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TRANSACTIONS & STUDIES

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Number 1 (April 1940)

Studies on Choriomeningitis and Poliomyelitis*

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CENTRAL nervous system diseases known to be or suspected of being caused by viruses are apparently on the increase and they constitute a puzzling group of ailments for the clinical diagnostician.

From time to time viruses have been described and identified as the causative agents for certain of these ailments and thus etiological classification is gradually evolving. Certainly these developments denote progress, yet, I fear that they have rendered the clinician's problem more complex rather than simplified it. Moreover, an etiological diagnosis in the individual case of central nervous system virus infection is often impossible on clinical evidence alone, but must rest upon laboratory findings. It is from this fact that I justify a laboratory worker's presumption in addressing this distinguished gathering of clinicians concerning certain recent developments relative to lymphocytic choriomeningitis and poliomyelitis.

* James M. Anders Lecture XV, The College of Physicians of Philadelphia, January 3, 1940.

LYMPHOCYTIC CHORIOMENINGITIS

The virus of lymphocytic choriomeningitis was first isolated and described in 1934 at the National Institute of Health (1) and has subsequently been isolated and identified in widely separated portions of the United States (1, 2, 3, 4, 5, 6, 7, 8) and in England (9, 10), France (11, 12) and Japan (13) and in Northern Africa (14) and there is clinical and serological evidence of its presence in Ireland (15). There are, moreover, considerations which make it appear probable that the virus is world-wide in distribution.

Choriomeningitis virus is now recognized to be the etiological agent responsible for some, but not all, cases which long since have been designated by such terms as aseptic or lymphocytic meningites.

The symptoms as described for etio-

logically established cases have varied considerably in character and in severity, although the isolated viruses have been immunologically similar with one exception. MacCallum, Findlay and Scott (16) studied two clinical cases apparently of choriomeningitis from which they isolated two strains of a virus which they have designated as pseudo-lymphocytic choriomeningitis. This virus, while suggesting choriomeningitis in its clinical and experimental manifestations in mice and monkeys, was found nevertheless to be immunologically distinct from it.

Symptoms. Lymphocytic choriomeningitis often has been noted to be preceded by upper respiratory symptoms (17, 18). These influenza-like symptoms usually improve but are followed in a few to several days by the sudden appearance of severe headache with fever, often accompanied by vomiting, stiff neck, and a positive Kernig's sign. In addition to these meningeal symptoms, somnolence, disturbances of deep reflexes, paralyses and anesthesias have been occasionally observed in etiologically established cases. These latter symptoms suggest the presence of an encephalomyelitis, for which reason Kreis (19) has criticized the designation "choriomeningitis" as being too restrictive in certain cases. Recovery is usually complete although sequelae, probably related to disturbance in cerebro-spinal fluid drainage, have been noted in certain cases. Barker and Ford's (5) case developed persistent symptoms which led to a laminectomy being performed when the pia-arachnoid space was found completely obliterated with fibrous tissue. A case reported by Armstrong and Sweet (7) made an apparently complete recovery and left the hospital, but following a prolonged bus trip to his home, developed repeated attacks of severe headache with vomiting. There were visual disturbances, associated with some blurring of the optic discs and the patient complained of difficulty in walking. These recurring attacks appeared over several months, but gradually lessened and ceased.

Pathology. There has been no pathological report from an etiologically proven case of choriomeningitis in man. The case reported from Philadelphia by Machella, Weinberger and Lippincott (20) was, however, clinically suggestive of this ailment and the pathological findings were similar in type to those observed in experimentally inoculated monkeys. In this case the meninges were infiltrated with lymphocytes and macrophages and were markedly thickened due to connective tissue multiplication with obliteration of the sub-arachnoid space. The brain substance was mainly not affected. The ventricles were distended, denuded of their ependyma, and there was a narrow subependymal zone where perivascular lymphocytic infiltration, glial proliferation, engorgement of vessels and hemorrhages were marked. The choroid plexus was partially necrotic and infiltrated with inflammatory exudate.

Pathology in Monkeys. In intracerebrally inoculated monkeys as described by Lillie (21) the lesions are characterized by an almost constant, irregular, more or less pronounced lymphocytic infiltration of the choroid plexus, some times with an exudate into the ventricles and by an almost constant, moderate irregularly distributed infiltration of the pia mater, and by few foci of glia cells and lymphocytic infiltration about the vessels. The cellular infiltrations may persist for a long time following the infection. The lungs often present congestion with intracellular oedema, serous exudation

and perivascular lymphocytic infiltration. Focal interstitial and perivascular accumulations of lymphocytes are frequent in various organs. The virus has been shown by Armstrong, Wooley and Onstott (22) to be widely distributed in abundance throughout the various organs and tissues examined from infected monkeys, namely, adrenals, cerebrums, blood, kidneys, liver, lungs, lymph glands, marrow, heart muscle, voluntary muscle, pancreas, spinal cord, spinal fluid, spleen, submaxillary glands and testicles, and in amounts not explainable by the presence of virus-containing blood in the vessels. The bile contained no demonstrable virus.

Pathology in mice, following intracerebral inoculation, shows the same type of meningeal infiltration as noted for the monkey, especially marked at the base of the brain, the lymphocytic infiltration of the choroid plexus with a resulting marked thickening being especially notable in this species.

When freshly isolated mouse strains are inoculated subcutaneously or intraperitoneally the animals develop marked difficulty of respiration and at autopsy the chest cavity is found filled with a clear virus-containing fluid, the spleen is enlarged to two or three times normal size and the liver and kidneys often show extreme grades of fatty degeneration. Lesions are entirely lacking when the neurotropic brain-transfer virus is similarly inoculated.

Host Range of the Virus. Many species have been found susceptible to experimental infection by the virus including man, chimpanzees (19), several types of monkeys, guinea pigs, white rats, eastern cotton rat (23), rice rat (23), white mouse (1, 3), gray mouse (1, 7) and the dog (24). Susceptible birds have not, to date, been detected although chickens, young chicks, canaries and pigeons have been found insusceptible (19). These results are of interest in view of the successful cultivation of the virus in the tissues of the developing embryo of the hen's egg by Bengtson and Wooley (25). The tissues of the inoculated embryo are rich in virus and many embryos died about the ninth to tenth day, although some of the eggs brought forth living chicks. Such chicks often appeared rather less active and rather somnolent but usually soon became normal. Laigret and Durand (26) report the finding of the virus in an uninoculated chick embryo, an extremely interesting observation if confirmed.

Cases in the District of Columbia. During a period of twelve months, four clinical cases of choriomeningitis were recognized in the District of Columbia. The diagnosis was confirmed at the National Institute of Health in three instances by isolation of the virus from the spinal fluid. In the fourth case spinal fluid was not attainable and the diagnosis was confirmed by establishing the absence of antibodies in serum drawn early in the attack and their presence in later samples.

In these four cases, as has been the rule in cases reported from other localities, there was no history of contact with any previous case; neither has a single instance of secondary infection been reported among the considerable number of relatives, associates or attendants exposed to established cases.

Reservoir of the Infection. The detection of spontaneous infection in several species of animals as white and gray mice, monkeys and in dogs, together with the absence of any apparent tendency for choriomeningitis to spread from person to person naturally suggests the possibility of the existence of an animal

reservoir for the infection. The homes of two cases were investigated with this possibility in mind and the virus of lymphocytic choriomeningitis recovered from gray mice trapped in each of them (7). The same results were secured with mice trapped in the homes of two additional cases (27). Trapping was next extended to homes in the neighborhood of recent cases and to other homes mainly in the poorer sections of the city. A total of 365 gray mice trapped in 76 different households was submitted to examination.

From this total, 303 mice were examined for the presence of virus by inoculating a pooled suspension of liver, spleen and kidney of each mouse intracerebrally into each of four white mice.* The inoculum consisted of .03 c.c. of an approximately 5 per cent organ suspension in saline. Strains of virus were recovered by this procedure from 64 gray mice, i.e., approximately one from each five mice examined was a carrier of the infection. These 64 infected mice were captured in 34 different homes from which a total of 122 mice were taken. In other words, 44.7 per cent of the homes in which mice were trapped were harboring infected mice and 52.4 per cent of the mice examined from these infected homes were active carriers of the virus.

Identification of Virus. The identification of the recovered virus strains was aided by observing the symptoms and the incubation period, both of which are rather characteristic in white mice. In addition, one or more brains from 46 lots of presumably infected sub-inoculated white mice were submitted to pathological examination by Surgeon R. D. Lillie, who reported the lesions of choriomeningitis as present in 44 of them, while in two instances pyogenic infection was the apparent cause of illness.

The final identification of any suspected choriomeningitis infection was made, however, by inoculating an emulsion of brain from one or more mice of the suspected group intracerebrally into four normal and four choriomeningitis immune mice. In every instance where the virus was considered to be present the immune mice all tended to survive while the non-immune mice all tended to die.

The detection of virus in gray mice by inoculating an emulsion of their organs into white mice is, however, subject to criticism in that stock white mice on several occasions have been found spontaneously infected with choriomeningitis virus and it is conceivable that our results were due to the presence of the infection in our stock white mice rather than in the gray mice which we had trapped. This is not believed to have been the case, however, since the same stock of white mice was being employed for other virus studies and in no instance was choriomeningitis virus detected. Moreover, it was noteworthy that the virus was repeatedly found in mice trapped from particular homes, while from other homes virus was consistently absent. This peculiar selectivity would hardly have existed had we been dealing with a random spontaneous infection of our mice colony. Moreover, in certain of the gray mice there were lesions suggesting choriomeningitis such as a pleural exudation, an enlarged spleen, or a fatty liver which enabled us to predict in a number of instances and later to verify the presence of the virus.

Immunity among Gray Mice. In or-

* A portion of the organs from each gray mouse was stored in 50% glycerine at approximately 4° C. in case it was desired for any reason to repeat the test.

der, however, to completely eliminate all possibility of any confusion due to the employment of white mice as test animals an experiment was undertaken, aimed not at recovery of the virus from gray mice, but at a determination of their immune status. Sixty-two gray mice trapped in 22 homes, where, according to our earlier tests the infection was present, were inoculated intracerebrally with 10–15 M.L.D.s of choriomeningitis virus. From these 62 mice there were 41 or 66.1 per cent which survived, while among 47 similarly inoculated mice trapped in homes where no infected mice had been found by our earlier studies there were but 5 survivors or 10.6 per cent, while 12 normal white mice employed as additional controls all died. The 62 gray mice tested for immunity were from homes wherein 83 mice had been trapped earlier and of which 37, or 47 per cent, had been found to be active carriers of the virus.

The results of the two methods are therefore confirmatory. The somewhat higher instance of the immune as compared to the carrier state suggests, as might be expected, that a portion of the mice had recovered from the infection but were still immune. Obviously since white mice were not employed in the immunity tests they could not possibly have confused the results.

Relationship of Cases to Mice. The finding of four human cases associated with 34 homes which harbored infected mice, while there were no cases among (42) homes which harbored non-infected mice or among a large but undetermined proportion of homes harboring no mice at all suggests that the infection passes between man and mice in either or both directions.

Man Probably Not the Reservoir for the Infection. It is difficult to consider man to be the reservoir of the infection in view of the ailment's apparent lack of tendency to spread from person to person. Furthermore, if man is the source of the infection we must assume that mice are highly susceptible to ordinary exposures of the virus. Experimental evidence, however, does not support this hypothesis. For instance, Kreis and also Findlay fed mice on highly infective tissues for from 8 to 11 days and found that only one mouse out of 4 or 5 became infected. Similarly, when well mice were placed in a jar containing experimentally infected mice, the latter being replaced as deaths occurred, Kreis found only 1 of 4 mice to have acquired the infection after an exposure of one to two months. These results are in accord with our experiences. It would, therefore, appear remarkable if our 4 human cases had in every instance infected the mice of their respective households.

Mice the Probable Reservoir for the Virus. The wider extent of the infection among mice as compared to man in the District of Columbia suggests mice as the reservoir of the infection. Nor does the apparent insusceptibility of mice to contact infection, as noted above, preclude this assumption, because as has been shown by Traub (28) a choriomeningitis infected mother transmits the infection to her offspring. Moreover, congenitally infected mice continue to harbor the virus for many months, whereas experimentally inoculated mice usually soon tend to rid themselves of the infection. The finding of 52 per cent of the mice from 34 infected homes to be carriers of the virus during the several months covered by our studies suggests a persistent type of infection among the mice which points toward the congenital type of the infec-

tion. Studies by V. Haas (29), moreover, indicate that congenitally infected mice may be more potent conveyors of infection by ordinary contact than are experimentally inoculated mice.

There are certain field observations also which point toward the mouse as the source of the human infection. For instance, Findlay, Alcock and Stern (9) record the development of symptoms soon after an individual had cleaned a shed overrun by mice. Wooley, Armstrong, and Onstott (30), moreover, noted the relatively higher incidence of protective antibodies among persons of the lower economic stratum of society and the four cases which we have studied in the District of Columbia were all from this group. These observations are in harmony with an hypothetical infection from mice, but hard to reconcile with a person to person concept for the infection.

How Does the Infection Pass between Men and Mice? The presence of the virus in the blood of the infected animal and the ready transmission of the systemic type of the infection through subcutaneous inoculations suggests the possibility of an arthropod transmission. We have attempted to transmit the infection by bed bugs, fleas and a blood-sucking mite but without success. The virus could be detected in each species when the engorged arthropods were emulsified and inoculated into normal mice within an hour following the infective feeding, but the virus was apparently no longer infectious after longer intervals. Attempts to transmit the infection through biting were entirely negative.

Coggeshall (31) reported the successful transmission of choriomeningitis to one guinea pig through the bites of 7 Aedes aegypti mosquitoes made five days after feeding upon an infected guinea pig. Shaughnessy and Milzer (33) succeeded in infecting Rocky Mountain wood ticks by feeding them upon infected animals and demonstrated that the infection could pass from larva to nymph to adult and to the egg, completing the cycle. Controlled biting experiments were not successful in conveying the infection but when infected nymphs were put in the cage with normal guinea pigs infection took place.

It is probable, however, that these observations have but little, if any, bearing upon the spread of choriomeningitis in nature, since proven cases appear throughout the winter in climates where active mosquitoes and ticks are scarce or absent during this period. On the other hand, no proven cases have been recorded for June, July and August, months when these arthropods are most prevalent in the northern hemisphere.

On the other hand, the early respiratory symptoms frequently noted in human cases suggest the respiratory tract as a possible route of infection. The case reported by Lépine of a laboratory worker who accidentally splashed some infectious material into his eye and in six days developed choriomeningitis is consistent with an upper respiratory route of infection as is the case reported by Findlay which developed the disease after cleaning a mouse infested shed. The virus escapes from infected animals by way of the urine and nasal secretions and it is possible that dust plays a part in the spread of the infection to man. It should be noted that experimental animals are susceptible to intranasal inoculation of the virus when freshly isolated strains are employed.

Why Are There Not More Human Cases? In view of the high incidence

of infection among mice in the District of Columbia, it is natural to inquire why more human cases have not become apparent. Some light has been thrown on this problem by the serum virus neutralization test on human sera. At the National Institute of Health some 1929 sera have been examined for the presence of choriomeningitis virus-neutralizing antibodies, of which between 12 and 13 per cent gave reactions indicating a definite immunity. An investigation of a considerable sample of these immune individuals showed that a history suggesting an attack of choriomeningitis or of any central nervous system ailment whatever was the extreme exception. This finding leaves two alternatives, either—1. The test is non specific and worthless or 2. Unrecognized infections with the virus occurs. The latter appears the more probable, because when susceptible animals are inoculated with the virus by routes other than directly into the central nervous system, illness results but invasion of the central nervous system is quite exceptional. That a similar occurrence is true for man is indicated by the human inoculations carried out in France (32) when a subcutaneous inoculation of the virus was followed in more than half the cases by only a systemic type of febrile attack resembling influenza or grippe. It is possible, therefore, that some, though certainly not all, cases diagnosed as "grippe" may in reality be due to infection with choriomeningitis virus. This possibility suggests an importance for the virus beyond what the occasionally recognized meningeal form of the disease would indicate. That there are not more cases of the latter is probably attributable to the efficient barrier which protects the central nervous system against infections of various types.

Special Considerations. The wide range of species susceptible to experimental inoculation with choriomeningitis virus, together with the detection of naturally infected mice, monkeys and dogs by several widely separated investigators, gives the virus an especial significance for those engaged in work with other viruses wherein animals are employed. Moreover, the tendency for choriomeningitis virus to be widely disseminated through the various tissues and organs of the infected host gives it an added importance for those engaged in research with or in the manufacture of tissue vaccines as attested on several occasions. For instance, Dalldorf and Douglass (24) recovered choriomeningitis from four different samples of dog spleens and found presumptive evidence of its presence in seven other instances. Needless to state, the unexpected appearance of this virus in their tissue transfers led to some temporary confusion in their canine distemper investigations. A commercial manufacturer, likewise, has encountered choriomeningitis virus in the preparation of canine distemper tissue vaccine and Mollaret (34) has raised the query as to whether this virus may not have been responsible for some of the meningeal reactions observed in the early attempts to vaccinate against yellow fever by means of mouse tissue vaccine employed in various manners.

Diagnosis. Choriomeningitis should be considered whenever an aseptic type of meningitis of undertermined etiology is encountered, even when the latter is associated with varying degrees of encephalitis or encephalomyelitis. The case reported by MacCallum and Findlay (10), moreover, suggests that choriomeningitis might well be considered in cases resembling poliomyelitis.

There is at present, however, no recog-

nized group of symptoms characteristic of central nervous system infection with this virus, while the clinical picture of the naturally occurring non-meningeal or systemic type of infection, which from indirect evidence almost certainly exists, has not as yet been recognized. The ultimate diagnosis in this virus infection is, therefore, dependent upon either the isolation of the virus or the demonstration of a developing specific immunity.

The virus is most readily recovered by the inoculation of spinal fluid or blood, drawn as early as possible during the febrile attack, into susceptible animals such as the white mouse or guinea pig. The inoculations should be promptly carried out, or when some delay is unavoidable the material for inoculation should be chilled. In our experience it is quite useless to inoculate animals with materials sent to the laboratory by mail.

A study of the serum for the development of specific immunity by means of the complement fixation test or the serum-virus neutralization test may also yield valuable information. Blood for these tests should be drawn with a strictly aseptic technique and handled without the addition of anticoagulants or preservatives of any kind. It is desirable that a sample of blood be secured as early in the attack as possible for the purpose of comparing its antibody content with later drawn samples.

Complement fixing antibodies are in evidence usually by the tenth day but fade rather rapidly following recovery. Virus-neutralizing antibodies, on the other hand, are usually not demonstrable before 6 to 10 weeks following onset and tend to persist for several months and in some instances for years.

Treatment. There is no specific treatment of proven value known. The experimental results of Rosenthal, Wooley and Bauer (36) in mice have not been consistent and when effective were dependent apparently upon administration before symptoms appeared, so that a favorable result is probably more related to prophylaxis than it is to treatment.

Special drainage has, however, been frequently found to give relief to the severe headache and vomiting. It should be pointed out, moreover, that cellular changes may persist in the spinal fluid for a considerable time following the disappearance of acute symptoms, and our experience at Washington suggests that there is danger in permitting the patients to leave the hospital before the spinal fluid has returned to normal.

Prevention. While there are many details of the exact method of spread for the virus yet to be determined, the findings reported do suggest that prevention would be served by the construction of homes with a view to rendering them mouse proof and by reducing or eliminating any existing mouse infestation from quarters closely associated with people.

THE EASTERN COTTON RAT AND THE MOUSE FOUND SUSCEPTIBLE TO THE LANSING STRAIN OF POLIOMYELITIS

In our considerations of choriomeningitis, we have been dealing with a virus capable of infecting a wide range of species and one that exhibits a tendency to invade many tissues and organs of the affected host. In poliomyelitis, on the other hand, we are dealing with a virus of extremely limited host range. Man alone of all animals has been proven to develop the disease in nature, and until recently, the only practical experimental animal available has been the monkey. The monkeys, however, are not ideal laboratory animals, since for their procurement we are largely de-

pendent upon a foreign market, the primary cost is high and the expense of housing and maintaining them is considerable. Moreover, the natural susceptibility of the monkey to such infections as tuberculosis and dysentery, together with the varying susceptibility of different individuals to infection by poliomyelitis, combine to further limit the usefulness of the monkey as a suitable laboratory animal for the study of this disease.

The finding of the Eastern cotton rat (35), a small hardy, inexpensive, easily reared and maintained animal to be susceptible, at least to certain strains of poliomyelitis is, therefore, of some interest.

The Lansing strain of poliomyelitis, the strain so far definitely adapted to the cotton rat, was isolated at the National Institute of Health from the spinal cord of a fatal case of bulbar poliomyelitis, one of several that occurred at Lansing, Michigan during the summer of 1937.* The patient, 19 years of age, died on August 26 with paralysis of respiration.

This strain of virus has been carried through fifteen monkey transfers and both clinically, and pathologically as reported by Surgeon R. D. Lillie, is apparently a typical strain of poliomyelitis.

With this strain, attempts were made to induce infection in several species of rodents. Some preliminary successes were secured in the Eastern cotton rat with fourth monkey passage virus in the fall of 1937 and winter of 1938. It was not until the summer of 1939, however, that we were able seriously to undertake the further transfers to this species which have led to the results herein reported.

* The material was secured through the courtesy of Dr. Max Peet, Department of Surgery, University of Michigan.

The virus has now been carried through twenty-seven consecutive transfers in the cotton rat, to which species it has become progressively better adapted. In the early transfers, the inoculations were not uniformly successful and the paralysis was often confined to but one leg. Affected animals which were not sacrificed tended to survive. Following the sixth generation, ninety-two cotton rats of various ages trapped in nature have been inoculated intracerebrally (.06 cc. of a 5.% brain and cord suspension), for purposes of carrying the strain. One of these 92 animals died on the fourth day following inoculation, possibly of poliomyelitis, while of the remaining ninety-one animals there has been but one which failed to develop flaccid paralysis. Animals not sacrificed now rarely survive. The incubation period has shown a tendency to stabilize at from three to five days and the pathological findings are more pronounced in later transfers. Paralysis of the extremities in all combinations has been noted as well as paralysis of the jaw and palpebral muscles. Death is usually due to respiratory paralysis.

Animals which survive develop marked atrophy of the paralyzed muscles and the overlying skin often loses its hair, whether due to a trophic change or to scratching or biting is not certain.

Emulsion of cord and brain from the third, sixth and fifteenth cotton rat transfer when inoculated intracerebrally into monkeys (1. cc. of a 5.% suspension) were followed by severe clinical and pathological poliomyelitis in all.

Three attempts at neutralization of the Lansing strain of virus have been undertaken in cotton rats, each employing poliomyelitis antisera received from Dr. E. H. Lennette, from Dr. Lloyd Aycock and one of our own from a

monkey recovered from an attack of poliomyelitis following inoculation with the P.M. strain of virus. These tests, while of a preliminary experimental nature, all indicate little or no protection with the Aycock serum, while with the other two a degree of protection is indicated by prolonged incubation periods as well as by failure of some of the animals to develop symptoms.

Attempts to adapt additional strains of virus to the cotton rat are under way. One rat inoculated with a strain of virus from the Niagara Falls outbreak of 1938 developed paralysis, first observed on the forty-first day. It is still too soon to know whether subtransfers with this strain will be successful or not.

Virus Successfully Passed to White Mice. Feeling that a strain of virus adapted to the cotton rat might be pathogenic for other rodent species, transfers to white mice were attempted. Negative results were obtained until the seventh cotton rat transfer of virus was employed, when one of five intracerebrally inoculated mice after an incubation period of thirty days was observed to be paralyzed in its left front paw and left hind leg. The following day the left front leg and both hind legs were completely paralyzed. Brain and cord material was inoculated into twenty-four white mice of various sizes, both Swiss and ordinary strains, and into cotton rat 353. Twelve of the twenty-four mice developed paralysis in one or more legs in from three to twelve days and the cotton rat developed typical symptoms on the eighth day and was completely paralyzed on the tenth day. The pathology as reported by Dr. R. D. Lillie was similar to that observed in direct cotton rat transfers.

Thirteen successive mouse transfers have now been accomplished and the virus is showing some tendency to affect a higher proportion of mice in later transfers. The incubation period is still quite variable, ranging from 2 to 20 days, but the majority of mice develop paralysis in from three to seven days. Death is now the rule in from 1 to 3 days following the onset of symptoms. In the absence of respiratory involvement, the mice attempt to eat, appear sleek and often without symptoms other than the paralysis.

Brain and cord emulsion from the fourth mouse transfer was injected intracerebrally into monkey 610, which developed a high fever that persisted from the fifth to eleventh days. The animal was nervous and tremulous, but recovered without paralysis. Monkey 618 was next inoculated with virus from the sixth mouse transfer and developed fever on the fourth day and tremors and definite weakness of the hind legs on the seventh day. The animal was sacrificed on the eighth day and a subinoculation of cord was made into monkey 620. This animal developed severe symptoms, followed by complete paralysis on the tenth day. Pathological lesions typical of moderately severe and severe poliomyelitis were reported for the respective animals by Pathologist J. E. Peers. An emulsion from the cord of monkey 620 was transferred to two cotton rats and to five white mice. Both cotton rats developed typical symptoms followed by complete paralysis. Three of the mice have to date developed paralysis and two have died. Pathological reports are not yet available.

Rhesus 621, inoculated with ninth mouse transfer of virus on December 11, 1939, after running a low grade fever and refusing food for several days, developed paralysis of both hind legs on December 30.

That the strain in mice is derived from the cotton rat strain is indicated by the successful transfer of the third, ninth and eleventh mouse generations of virus again to cotton rats with the development of characteristic symptoms and pathology for this species. Moreover, it is now possible quite regularly to induce the infection in white mice through the direct transfer of brain and cord from infected cotton rats. Direct primary mouse inoculations from the fourteenth, fifteenth, sixteenth, eighteenth, nineteenth, twenty-fourth and twenty-fifth cotton rat transfer have uniformly produced flaccid paralysis in a portion of the inoculated mice.

The pathological lesions in cotton rats, and in the mice as far as studied, are similar in type to those observed in poliomyelitis of man and of experimental animals.

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The Vitamin B Deficiencies*†

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IT SEEMED to me that the College of Physicians of Philadelphia wished to stress particularly the importance of certain recent advances in the medical sciences when they honored me with an invitation to be the Mary Scott Newbold lecturer. Therefore, I have chosen as my topic, "The Vitamin B Deficiencies."

The advances in the science of nutrition, like those in most branches of science, have resulted from the work of a large number of investigators. For whatever contributions I have been able to make to our knowledge of dietary deficiency diseases, I am indebted to a large number of associates and philanthropic persons from whom I have learned and received so much.

My chief, Professor M. A. Blankenhorn, feels strongly that problems should arise in the mind of the medical investigator from his experience in the clinic, and he suggested that I tell you why I chose to make special studies in this particular field. My first interest in nutrition came when, as a small boy in Texas, the mother of one of my playmates died from pellagra. At that time, pellagra was endemic and recurred frequently in the South. Each year a number of our neighbors became insane or died from this disease. While in medical school, I saw a case of pellagra and took the opportunity of reading Casal's original shrewd description of the disease, dated 1735. Since Casal's time, hundreds of observers have contributed to our knowledge of pellagra, but an outstanding contribution was made by Dr. Joseph Goldberger and his associates. They learned that pellagra could be prevented by diet and believed they could treat it successfully by dietary measures. They thought, too, that they had produced by dietary restriction a disease in dogs (canine blacktongue) and in rats (rat pellagra) which was analogous to human pellagra.

My next association with pellagra came in the summer of 1930 when I began my interneship at the Lakeside Hospital in Cleveland, Ohio. One of my first patients was a pellagrin and, although I gave him the therapy recommended by Goldberger, within forty-eight hours the patient was dead. His death was naturally a shock to me. I consulted all of the case histories of pellagrins who had been admitted to the hospital and found the death rate to be fifty-four per cent. I then learned that there was a similar high mortality rate in the leading institutions throughout the United States, despite the fact that they were using what had been thought to be specific dietary therapy. Dr. James S. McLester of Birmingham, Alabama, and Dr. C. C. Bass of New Orleans had, for

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many years, continued to point out that irrespective of whether or not Goldberger's method of treatment was prescribed, the death rate among pellagrins admitted to the hospital remained approximately the same. It occurred to us that perhaps the quantity of the therapeutic agents recommended supplied an adequate amount of the antipellagric factors to prevent the disease but not to cure it. To test this hypothesis, we selected pellagrins admitted to the hospital, and to a group of very severely ill cases administered much larger doses of yeast or wheat germ and a more liberal diet than had been recommended previously. Every detail of treatment was supervised. On this therapy, the death rate fell from fifty-four per cent to six per cent, and we were convinced that the former frequent failure to respond to therapy had been due to the inadequate amounts of the therapeutic agents administered. Another selected group of pellagrins was restricted to a pellagra-producing diet—the most deficient in vitamin B complex factors which we could devise—and observed under controlled conditions. These patients, if kept at rest, often showed improvement in some of the symptoms while restricted to this diet. The pellagrous dermatitis usually healed, but invariably the patient lost weight and oftentimes the pellagra would recur. After much study, we learned that pellagrous glossitis, which remained unchanged or became worse during a period of several days' observation, could be used as an index for testing the potency of a potential therapeutic agent, whereas the skin lesions, which are never static, were shown to be unreliable. This observation prompted us to administer identical diets to pellagrins and to young rats. Miss Jean M. Grant and I learned that a pellagra-producing diet, on which the skin lesions of a pellagrin healed, produced the so-called vitamin G deficiency of Goldberger. We concluded that since the skin lesions of human pellagra healed on this diet, the dermatitis of pellagra and the skin lesions of rat pellagra were not identical. This point has now been settled beyond any reasonable doubt. From our early studies, we observed also that ventriculin and liver extract, which are efficacious in the treatment of pernicious anemia, were likewise effective in the treatment of pellagra and of this condition in the rat. We then demonstrated that the gastric juice of pellagrins, unlike that of patients with pernicious anemia, contained the intrinsic factor of Castle.

At Lakeside Hospital in Cleveland, we dealt chiefly with pellagra associated with chronic alcoholic addiction. Accordingly, in 1931, we began a study of the relationship of alcohol to the development of pellagra. Our investigations showed that the peripheral neuritis, disturbances of the alimentary tract, and various other manifestations occurring in these pellagrins disappeared when the patients were treated with large amounts of a well-balanced diet, yeast, or liver, in spite of the fact that the patients continued to drink between a quart and a quart and a half of whiskey per day. These symptoms did not recur so long as the patient continued this treatment, even though he still drank excessive amounts of alcohol. At this time, we advanced the hypothesis that so-called "alcoholic pellagra" was a form of true pellagra. By the end of 1934, we had treated 125 severely diseased "alcoholic" pellagrins, with a decrease in death rate from fifty-four per cent to six per cent. This decrease was due to the development of better methods of therapy described above. We also learned that liver ex-

tract when injected in large amounts was an effective anti-pellagric material and was often life-saving.

Dr. J. S. McLester visited our clinic in Cleveland and pointed out that the death rate in their series in Birmingham was high, irrespective of whether or not the Goldberger method of treatment was applied. Naturally, he wondered if the pellagra of the north and that of the south were the same. He invited us to the Hillman Hospital in Birmingham to study pellagra in an endemic area. During the spring and summer of 1936, we applied our therapeutic methods to fifty cases of severe endemic pellagra in Birmingham, a high percentage of which were literally at the point of death. Three patients died, and at postmortem all revealed adequate explanation for death aside from residual lesions of pellagra (the acute manifestations had disappeared prior to death). The remainder recovered. Since alcoholic and endemic pellagra responded similarly to identical therapy, we were convinced that the two were the same disease.

In September, 1937, Elvehjem, Madden, Strong and Woolley announced improvement in dogs with canine blacktongue following the administration of nicotinic acid and nicotinic acid amide. We had nicotinic acid in our possession and tried to find something in the medical literature concerning its toxicity. Nothing had been written. Eventually, with all due care, we tested the material on ourselves and found that it was safe. We then administered the material to four pellagrins who improved spectacularly. These results formed the basis of our first report, read November 5, 1937, at the meeting of the Central Society for Clinical Research, at which we reported that the administration of nicotinic acid and nicotinic acid amide to ourselves, other volunteers, and patients caused no harmful effects, and, when given in adequate amounts to pellagrins, was followed by dramatic improvement in the mental symptoms and disturbances of the alimentary tract. S. P. Vilter and I demonstrated that normal persons ingesting a well-balanced diet excrete a considerable amount of nicotinic acid or substances similar to it, whereas pellagrins in relapse excrete much less. We were also able to show that red, ether-soluble substances in the urine of pellagrins in relapse disappeared following treatment with nicotinic acid. These substances are not excreted by dogs with blacktongue who eat scraps from the food eaten by pellagrins.

Turning to our recent investigations, I have in mind a case representative of many studied in our clinic. This patient is a fifty year old white man whose two brothers and six children had symptoms of subclinical mixed deficiency disease. Such symptoms are loss of appetite, weight and strength; indigestion; constipation; occasional attacks of diarrhea; abdominal cramps; burning of the tongue, corners of the mouth and stomach; burning and itching of the eyes; periods of burning, itching and crawling sensations over the skin; excessive nervousness; increased fatigability; insomnia; dizziness; forgetfulness and confusion. The soles of his feet burned and the muscles of his legs often became cramped. These symptoms we now know are the prodromal symptoms of clinical pellagra, clinical beriberi, clinical riboflavin deficiency and other associated deficiencies. They usually appeared in the spring and fall, and each year became more severe. Early in 1938, he developed lesions characteristic of clinical pellagra which disappeared following nicotinic acid therapy. He

continued to take large doses of nicotinic acid, but his inadequate diet remained unchanged and subsequently he was treated specifically for the following distinct deficiency syndromes: beriberi, riboflavin deficiency, scurvy, vitamin B_6 deficiency, vitamin A deficiency and anemia. The effect of specific therapeutic substances on patients with the corresponding deficiencies will be discussed separately.

1. Nicotinic Acid and Nicotinic Acid Amide

Nicotinic acid and compounds acting similarly play an important part in the basic physiological functions of man. Their administration in adequate amounts:

1. Increases the content of coenzymes I and II in the blood and urine in vivo. In the presence of added nicotinic acid amide or nicotinic acid, the in vitro synthesis of these coenzymes by defibrinated blood has also been observed in this laboratory, and from our experiments it seems that the red cells store and carry the enzymes and white cells synthesize them.

2. Increases the nicotinic acid content of the blood and urine of normal persons and persons who have a nicotinic acid amide deficiency. Such a deficiency exists in persons who have pellagra, and frequently in those who have diabetes mellitus, infections, chronic diseases, and malnutrition from any cause.

Following the administration of these substances, unexplained phenomena in regard to hair growth and hearing have been reported by some persons. A few persons who had had a noticeable loss of hair have observed a striking increase in the growth of hair. Two of the many older persons treated stated that while their hair had been gray for a number of years, the color of the new hair was similar to what it had been when they were fifteen or twenty years of age. A few persons who did not hear well have had spectacular improvement in hearing.

3. In cases of subclinical pellagra, they (a) Increase appetite, strength, and feeling of well-being. (b) Relieve indigestion, diarrhea, burning of the tongue and stomach, burning and itching of the skin, dizziness, forgetfulness, confusion and insomnia. (c) Cause the abnormal ether-soluble red pigments to disappear from the urine of pellagrins and persons with malnutrition.

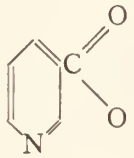
4. In cases of acute or relapsed pellagra, whether the disease is endemic or secondary to organic disease or chronic alcoholic addiction, the administration of these substances will: (a) Cause fading of the fiery red lesions of the mucous membranes and strikingly diminish the Vincent's infection associated with it. (b) Restore to normal deranged mental functions, provided they result from pellagra. (c) Cause the disappearance of ether-soluble red pigments from the urine of pellagrins. (d) Revive the appetite and restore normal alimentary function, sometimes with a return of gastric HCl. (e) Increase strength and restore feeling of well-being. (f) Cause fading of the dermal erythema but not cure the residual changes of the skin.

5. Nicotinic acid has no specific effect on peripheral neuritis, anemia, or symptoms of vitamin A, vitamin C, riboflavin, vitamin B_6, or adenylic acid deficiencies.

6. Since very small amounts of yeast and liver extract increase the efficacy of nicotinic acid, it is possible that nicotinic acid operates in conjunction with protein fractions and other active principles.

Vasomotor Reactions of Nicotinic Acid. As was pointed out at the time nicotinic

acid and its amide were reported of specific value in the treatment of canine blacktongue, there was no information regarding the pharmacologic activity of these pyridine compounds in man. It has been found that when nicotinic acid is given orally or parenterally in large amounts, a sensation of heat, itching and tingling, together with flushing of the skin, frequently occurred. Dr. W. B. Bean and I have studied this phenomenon very carefully on 47 adult males, 7 females and 4 children. Each test was made when the subject was in the post-absorptive state. For one to two hours before the test, the subject was placed flat in bed in a constant temperature room (20°). It was soon discovered that the most extensive vasodilator effect of nicotinic acid and its compounds occurred in the face and neck. Dr. Bean and I have learned that the vasodilator effect of the pyridine compounds studied is a highly specific function of only such of them as contain the free structure.



All compounds tested in which one of the ring hydrogens had been substituted or in which an addition had been made in the ring nitrogen were inactive. Pyrazine derivatives have little tendency to produce vasodilatation. Since satisfactory results have been obtained in treating pellagra with nicotinic acid amide and other drugs, it is obvious that the molecule potent in the treatment of pellagra is not the same as that producing the vascular reaction. All pyridine compounds that we have tested which produce the skin changes are potent in the treatment of pellagra. The discovery of a skin vasodilator as innocuous, effective and cheap as nicotinic acid naturally suggests many uses in addition to its use as a vitamin. It perhaps may be of value for its local circulatory effect. However, the use of it in peripheral vascular disease should be discouraged since it seems to decrease blood flow in the limbs.

II. Thiamin Hydrochloride (Vitamin B_1)

Thiamin hydrochloride is probably important to all cellular life and is certainly important for the normal function of the nervous system. The administration of thiamin:

1. Increases the vitamin B_1 and co-carboxylase content of the blood and urine of normal persons and of persons who have a deficiency of thiamin.

2. In cases of subclinical thiamin deficiency: (a) Often increases appetite, strength and feeling of well-being. (b) Relieves the symptoms arising from the early neurological lesions of beriberi. (c) Relieves the initial nervous syndrome of beriberi (anxiety neurosis). This includes hyperesthesia to all forms of stimuli, increased psychomotor drive, increased emotional drive with a definite trend toward depression and apprehension, weariness, increased fatigability, headaches, and sleeplessness. (d) Often causes the widely dilated pupils frequently seen in malnourished persons to return to normal.

3. In acute beriberi: (a) Relieves the pain and improves the strength, accuracy and speed of movement. (b) Relieves tenderness of nerve trunks, reduces muscle excitability and improves strength of grip. (c) Improves the advanced neurological lesions of beriberi. In rare instances, the disease reaches a stage in which degenerative changes are irreversible. (d) Restores to normal the

electrical conductivity of peripheral nerves. (e) Relieves the central and peripheral cardiovascular disturbances. These include edema, cardiac dilation, speeded circulation, high venous pressure, and prolonged electrical systole.

4. Improves gastrointestinal function in thiamin deficient patients.

5. Increases carbohydrate tolerance and improves carbohydrate metabolism in thiamin deficient patients.

6. Increases bisulfite binding substances in the blood.

7. May have the following additional functions, although they are not yet fully established: (a) Essential for normal growth, appetite, and gastrointestinal motility. (b) Reduces symptoms of withdrawal in morphine addicts. (c) Relieves pain in neuritis of leprosy (ischemia at rest)?, tabes, herpes zoster, amputation neuralgia, tic douloureux, and facial paralysis.

III. Riboflavin

Riboflavin is probably essential to all cellular life and important in carbohydrate and protein metabolism. The administration of riboflavin:

1. Increases the excretion of riboflavin in the urine of persons with riboflavin deficiency and of normal persons.

2. In subclinical cases of riboflavin deficiency: (a) Increases strength and feeling of well-being. (b) Relieves burning of lips and itching and burning of skin around the mouth and eyes and over the nose.

3. In ariboflavinosis (riboflavin deficiency): (a) Cures chielosis (lesions at corners of mouth), erosions around eyes, "sharkskin" lesions of the nose (sharkskin appearance of skin over nose). (b) Improves general condition and vigor. (c) Increases sense of well-being. (d) Relieves patient of ocular symptoms (see section on ocular symptoms).

4. Increases efficacy of nicotinic acid in certain pellagrins.

5. May have the following additional functions but they are not yet wholly established: (a) Increases weight and appetite. (b) Is essential for growth. (c) Spares thiamin.

IV. Vitamin B_6

The administration of vitamin B_6 to selected persons who are deficient in this vitamin: 1. Relieves extreme nervousness, insomnia, irritability, abdominal pain, and difficulty in walking. 2. Relieves cramping pains in stomach and stimulates appetite. 3. Causes improvement in some patients with idiopathic epilepsy. Dr. W. B. Bean and I have observed improvement in about two-thirds of the cases studied. 4. May benefit patients with amytrophiclateral sclerosis. Dr. E. Roseman, Dr. C. D. Aring and I saw one patient who was benefited by this treatment, and the author has seen another who improved strikingly. The author also has seen three cases of myasthenia gravis which showed striking improvement within twenty-four to forty-eight hours after the injection of vitamin B_6, and two cases of amytrophiclateral sclerosis which were benefited by synthetic (Merck) vitamin E. 5. Relieved pain in two patients with combined system disease. 6. Produced a definite but small rise in reticulocytes in macrocytic anemia (H. S. Schiro and R. W. Vilter). There was no increase in red blood cells. This substance is certainly not the anti-pernicious anemia factor. 7. Caused relief in one case of arsenic neuritis (Vilter and Spies). Vitamin B_1 had previously been administered for three weeks without beneficial effect. The administration of vitamin

B_6 in normal saline was followed by great relief which lasted for three days; then the symptoms returned. Saline had no effect, but when crystals of vitamin B_6 were added, relief again followed.*

V. Vitamin A

The administration of vitamin A in the form of carotene or oleum percomorphum to persons with vitamin A deficiency: 1. Relieves burning of eyes, photophobia, and conjunctivitis (see ocular symptoms). 2. Enables these patients to see well enough to read with greater ease. 3. Relieves xerophthalmia and increases visual acuity especially at night.

VI. Vitamin C

The administration of cevitamic acid to persons with scurvy: 1. Cures the swollen bleeding gums and the ulceration and hemorrhages of the mucous membranes of the mouth and the mucous surfaces elsewhere. 2. Relieves the pain, tenderness and swelling in the joints. 3. Stops hemorrhages of the skin. 4. Increases strength and sense of well-being.

VII. Adenylic Acid

Poorly nourished persons who have symptoms that have not been relieved by nicotinic acid, thiamin hydrochloride, oleum percomorphum, riboflavin or vitamin B_6 have, in some instances, been treated with adenylic acid.

Dr. Bean and I first gave this substance intravenously, in small amounts, to eight normal persons. Later we gave as much as from 3 to 20 milligrams, dissolved in sterile physiological solution of sodium chloride. Within fifteen seconds after the injection, the subjects had involuntary, deep, gasping inspiration, fluttering in the upper part of the abdomen, and a feeling of fullness in the head. All patients had transient flushing of the neck and face, and the pupils became widely dilated. The arterial blood pressure fell slightly, and the heart rate increased. All symptoms vanished within 3 to 5 minutes after they began and left no evidence of harmful effect. The administration of a single dose of 200 milligrams of adenylic acid by mouth produced similar but less intense symptoms in about one-fourth of the persons treated. Adenylic acid was then given to a series of pellagrins in relapse, and it was found that nicotinic acid and adenylic acid, administered together, were more effective than nicotinic acid alone. Persons with malnutrition who complained of intense burning of the oral mucous membranes but who showed no diagnostic evidence of pellagra were, in six instances, relieved following treatment with adenylic acid alone, whereas placebos similar in appearance produced no relief. While this compound is of great interest to us, we do not recommend at this time that it be given to human beings as a therapeutic agent.

The case described illustrates the extremely important concept that nutritional deficiencies exist as complexities and not as single entities (see schematic illustration I). Controlled studies on this patient and his family show that some of the deficiencies, and presumably all in endemic cases usually begin in infancy and childhood if, in fact, they do not develop in utero. The manifestations of the disease in infancy and childhood

* It is too early to say whether or not these observations are specific and apply to more than the cases described, but evidence indicates that synthetic vitamin B_6 and synthetic alpha-tocopherol benefit the patient more than either alone. Considerable study is necessary before conclusive statements are warranted.

are very different than they are in an adult, but a therapeutic test is of great value in confirming the diagnosis. Controlled studies on this patient showed that he had seven distinct deficiency diseases. The pellagra responded to the administration of nicotinic acid; beriberi, to thiamin hydrochloride; riboflavin deficiency, to the administration of riboflavin; vitamin B_6 deficiency, to synthetic vitamin B_6; vitamin A deficiency, to oleum percomorphum; and scurvy, to cevitamic acid. Still other symptoms were relieved by adenylic acid. Needless to say, the more accurate the initial diagnosis of the specific deficiency disease, the more likely is the physician to avoid futile treatment with unnecessary preparations. The details of therapy have been described recently. The following special features which were prevalent in this case and in many others need special consideration:

MENTAL SYMPTOMS

We have shown in a study of two hundred patients with acute psychoses of pellagra that the abnormal signs and symptoms are relieved dramatically following therapy with nicotinic acid, nicotinic acid amide, or sodium nicotinate. Clinical improvement is associated with specific chemical changes. Soon after the administration of the specific therapeutic agent to a pellagrin with acute psychoses, the concentration of coenzymes I and II in the blood increases. Since these enzymes are fundamental to carbohydrate metabolism, the association seems especially significant. We have also demonstrated that pyrazine monocarboxylic acid, pyrazine 2,3-dicarboxylic acid and quinolinic acid, substances which are different in chemical structure from nicotinic acid and which were thought to be physiologically inert, are effective in the

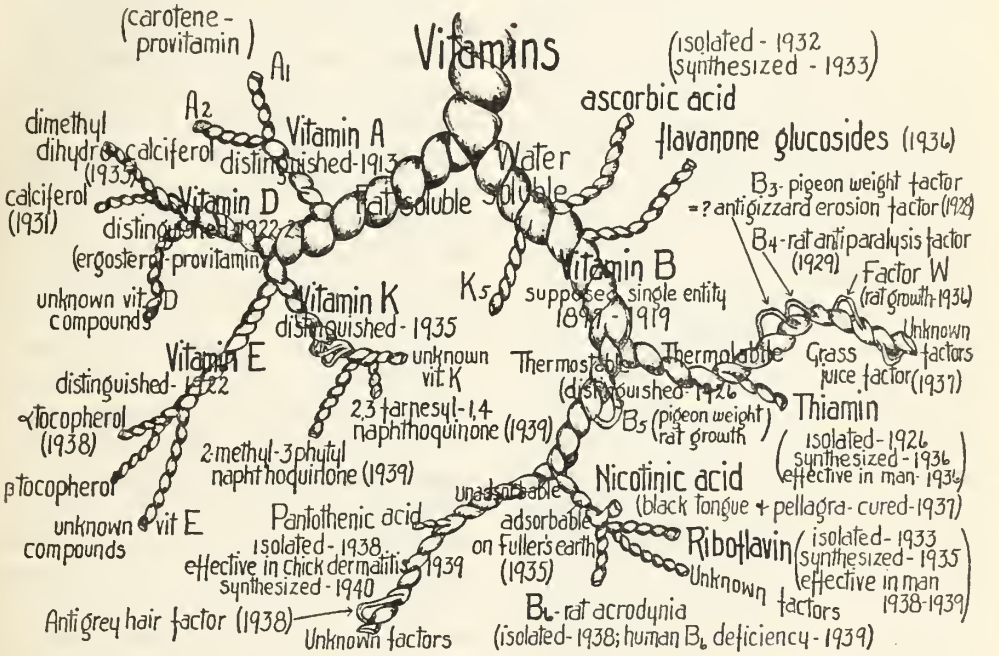


ILLUSTRATION I

treatment of acute psychoses and other signs of pellagra.

We have observed relief of the chronic psychoses of pellagra in patients who had been committed to custodial mental institutions for as long a period as nine months. Recovery, in some cases, was complete and there was no recurrence of symptoms so long as the patient remained on a well-balanced diet, supplemented with nicotinic acid. Patients whose psychosis was of longer than nine-months' duration showed improvement to the extent that those who were bedridden became ambulatory and were able to feed and care for themselves. However, we were unable to effect a complete cure of the psychic changes. Additional study is required as many of these patients probably had some other serious mental disturbance, such as schizophrenia, and developed secondary pellagra because they refused to eat. We were not confronted with this problem in our study of pellagrins with acute psychoses, as we had followed such cases for long periods of time and had established the fact that other manifestations of pellagra preceded the development of their mental symptoms.

Dr. J. P. Frostig and I have learned of an initial nervous syndrome associated with pellagra, beriberi, and other related diseases. This syndrome has been diagnosed in the past under the heading of neurosis, particularly anxiety neurosis, and is often associated with a disintegration of the personality, including a breakdown of morale. The symptoms of this initial nervous syndrome are hyperesthesia to all forms of sensation, increased psychomotor drive, increased emotional drive with a definite trend toward depression and apprehension, weariness, increased fatigability, headaches, and sleeplessness. These symptoms are uniform but have no connection with the single personality.

Treatment with large amounts of nicotinic acid, cocarboxylase, or vitamin B_1 is followed by rapid relief from these symptoms. Riboflavin or vitamin B_6, however, do not produce the same effect. The latter substance does have a sedative effect.

OCULAR SYMPTOMS

More than seventy per cent of the patients in the nutrition clinic who have frequent recurrences of pellagra, beriberi or riboflavin deficiency have visual disturbances. Unless their diets improve, their ocular manifestations become more severe and are characterized by severe burning, itching and excessive dryness of the eyes; photophobia; granulation; and extreme redness of the conjunctiva, particularly of the lower lids. The whole symptom complex is extremely variable from one patient to another and, as a rule, disappears in the late summer and returns again in the early spring. Following the daily administration of vitamin A, in the form of carotene in oil or as oleum percomorphum, in amounts ranging from 10,000 to 50,000 units, some of these patients were able to read better, the burning ceased, and the conjunctivitis and photophobia disappeared. In many other cases, photophobia and conjunctivitis were relieved following the oral or parenteral administration of 3 to 5 milligrams of synthetic riboflavin or by small amounts of milk, liver or brewers' yeast.

Whether these ocular manifestations are due to a lack of either vitamin A or riboflavin, or both, the condition is probably associated with a mild keratitis. The symptoms wax and wane with the seasons, and for that reason perhaps there is not a tremendously high incidence

of these lesions fully developed. A deficiency of riboflavin and vitamin A is almost certain to exist in the year-round diet of many persons in India. Could it be that the great masses of population of India who have eye disease are suffering from a deficiency of one or both of these substances?

ETHER-SOLUBLE RED PIGMENTS

Some years ago, we described a simple method for detecting small amounts of porphyrin in the urine. We thought at that time that the color was specific for the presence of porphyrin, but we now know, through the work of a considerable number of investigators, that a number of pigments can give a positive test and that this test is not specific for porphyrin. When a person with malnutrition, whether or not he has clinical pellagra, excretes increased amounts of these pigments in the urine, we consider the test positive. We now know that this test rapidly becomes negative after treatment with yeast, liver, nicotinic acid, or quinolinic acid. Similar, if not identical pigments appear after roentgen sickness and are present in many people who have chronic diseases. Dr. W. B. Bean and I recently studied 62 malnourished patients at the Cincinnati General Hospital, none of whom had clinical evidence of pellagra. Some of these people ingested amounts of a well-balanced diet sufficient for the average person; others ate an unbalanced diet; and still others had disorders of the alimentary tract and it is doubtful if they could have had normal utilization and absorption of food. Another group had prolonged fever or hyperthyroidism. A smaller group had cardiac decompensation with congestion of the liver; others had diabetes mellitus or chronic nephritis with uremia. The urine from forty-five of these cases showed a positive test. Within two months, 18 of the patients had developed diagnostic signs of pellagra and a number of them had symptoms of beriberi and riboflavin deficiency. Within twenty-four hours after therapy with nicotinic acid, all patients, whether or not they had diagnostic clinical evidence of pellagra, had a great increase in sense of well being and responded in a manner similar to subclinical pellagrins we have already described. Accordingly, we feel that this test is simple and useful in the recognition of early states of malnutrition, but that it is not a specific test for porphyrinuria. It is particularly useful in indicating that certain patients who had not hitherto been considered as dietary problems need special dietary therapy.

HOMEOSTASIS

The more one studies these deficiency diseases, the more he is impressed with the great factors of safety operating to protect the body so far as these essential substances are concerned. We see that life may continue long after the deficiency state sets in, and there is always a margin of safety between the beginning of ill health and death from these diseases. When function of the tissues of these patients is diminished or altered due to a deficiency over long periods of time, there is quick restoration of function following the administration of adequate amounts of the specific missing material or materials. Nevertheless, following deprivation of these substances from the diet, there is a limit to the self-regulation and, indeed, at times, to the repair which is possible as a result of therapy. Nicotinic acid amide, thiamin hydrochloride, and riboflavin must come to the human body from an external source, and since the body does not conserve all of these

materials, one should, when treating persons who have these specific deficiency diseases, insist upon as little activity as possible on the part of the patient until repairs to affected tissues are under way. So far as we can tell, these agents serve in a natural manner to perform a natural function which becomes interrupted or altered when inadequate amounts of these specific substance or substances are available. It has been our experience that the more severe the deprivation, the greater the response of the patient to specific therapy. Studies on several thousand patients have forced us to conclude that the blood concentration, within wide limits, for each of these materials is constant, even though various tissues may be robbed to maintain this concentration. The patient adjusts rapidly, even in the face of severe disturbances either in internal or external conditions, for if too much material is given and the body is already amply supplied, it rapidly overflows into the urine. Likewise, when patients have ingested sparingly and periodically, the material can be stored to a limited degree and can be called upon for immediate usage. Failure on the part of the physician and investigator to understand these fundamental principles accounts for some of the wide differences of opinion and variations in the description of deficiency diseases. To be more specific, when the supply of nicotinic acid amide or substances which act similarly to or in conjunction with it is inadequate, it seems that, after a time, the cell functions improperly and the storage depots are called upon to maintain as best they can. Eventually, if the intake is not increased, characteristic lesions of pellagra may appear. While the sequence of appearance of these lesions is constant for each recurrence of the disease within the same person, it may vary tremendously from person to person. A similar situation arises when beriberi develops as a result of a deficiency of thiamin, and riboflavin deficiency appears because of an inadequate supply of this substance.

In the treatment of deficiency states, we long ago pointed out the desirability of rest for the patient. We reported that in many cases the lesions healed following rest in bed. More recently, we have been able to demonstrate that with the diet remaining inadequate and with no administration of specific therapeutic agents, there is a significant increase in the blood concentration of these coenzymes if the patients remain at rest in bed. This may well explain why investigators who examine their patients at the time they are admitted to the hospital obtain different levels in the blood and urine from those who wait until after the patient has been in bed, when the blood concentration of coenzymes I and II is almost certain to have reached a lower metabolic level. Likewise, differences may well appear when the physician and investigator fail to realize that the fluid matrix which contains the cells and transports these materials may be in itself extremely variable and even small red blood cells may contain more of these fundamental enzymes than larger red blood cells so that a hematocrit reading might not in itself give all the information one would desire.

When one considers the importance of these vitamins in carrying out the essential processes of life, many of the apparently contradictory phenomena concerning these deficiency diseases are easily reconciled. (Many factors other than diet may contribute to the deficiency; absorption from the alimentary tract and utilization by the liver and other tissues are of great importance.) Increased metabo-

lism due to rapid growth, increased exercise, infectious diseases, pregnancy, and hyperthyroidism may each play an important part in the appearance of symptoms and may even obscure, in some instances, the early manifestations of the deficiency disease.

In our clinic, we find that the unbalanced and inadequate diets eaten by the majority of patients may predispose each of them to a number of nutritional disorders, and we insist that the diagnosis of one clinical syndrome necessitates a thorough search for others.

SUMMARY AND CONCLUSIONS

In the clinic at the Hillman Hospital, we have treated 1250 ambulatory persons with pellagra and associated diseases without a fatality. While treating these persons, often under controlled conditions, we have evolved methods which make possible an earlier diagnosis and more effective therapy, with the result that persons will be saved the months and years of ill health which ordinarily exist from the time deficiency diseases start until they become recognized. We have a clearcut demonstration that infants and children in the endemic areas are affected by these diseases in forms which have not heretofore been recognized. These observations have also led to the discovery of entirely new deficiency diseases and methods of treating them.

Among some of the new and unpublished observations are that following the daily administration of 50 milligrams of synthetic vitamin B_6 (2-methyl, 3-hydroxy, 4,5-di[hydroxymethyl]pyridine) to persons having macrocytic anemia of pellagra or pernicious anemia in relapse, a slight but definite reticulocytosis occurs, and that in such patients having leucopenia, there is a definite increase in the polymorphonuclear series of white cells. We have also learned that vitamin B_6 may have a sedative effect when administered in this dosage either to normal persons or to persons with deficiency disease. Dramatic but temporary improvement followed the administration of this substance to a person with arsenic neuritis and to a few persons with idiopathic epilepsy. The majority of persons with epilepsy, however, showed only slight improvement or no improvement whatever.

A number of chemical compounds, such as pyrazine monocarboxylic acid, pyrazine 2,3-dicarboxylic acid, and quinolinic acid, which were formerly considered physiologically inert, we now know are potent in the treatment of some of the diseases arising from malnutrition.

From our experience, we have learned that we must search for mixed rather than single deficiencies; that subclinical deficiency states may exist for years before diagnostic lesions appear and that such cases, if a positive therapeutic test is obtained, should be treated with a liberal well-balanced diet supplemented with the specific therapeutic agent or agents indicated. We have learned also the importance of giving supplements of the water-soluble vitamins to all undernourished persons receiving large amounts of carbohydrate. In treating mixed deficiencies, brewers' yeast and liver are invaluable therapeutic agents and they contain a number of active principles other than those discussed in this paper. A very satisfactory and effective method of administering dried brewers' yeast (Anheuser-Busch, Inc.) was found by combining it up to twenty-five per cent with peanut butter.

We have observed that the abnormal signs and symptoms of acute pellagrous psychoses are dramatically relieved

following the administration of nicotinic acid or one of its compounds. Soon after the administration of one of these therapeutic agents, the concentration of coenzymes I and II in the blood increases dramatically and parallels the general clinical improvement. The chronic psychoses in pellagrins who oftentimes have been committed to custodial mental institutions diminish greatly in severity following the administration of nicotinic acid if the psychosis is caused by pellagra and, in some instances, the persons have returned to normal. In all cases, there was great improvement; often the person after being bedridden became ambulatory.

We have described an initial nervous syndrome which is associated with a disintegration of the personality.

As has been pointed out in our discussion, these specific deficiencies occurring from deprivation of water-soluble vitamins are interrelated, and probably the same biochemical system or systems are involved. The more one studies these diseases, the more he is impressed with the factors of safety operating to protect the body so far as these essential substances are concerned.

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The History of Disease among the Natives of Alaska*†

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THE discovery of Alaska in 1741 by the Russian Chirikoff was followed within several years by further explorations, and by numerous hunting and trading expeditions. Contact between the Russians and natives, at first more or less casual, became more intimate and constant as trading posts and settlements were established. The first of such settlements was founded in 1784 on Kodiak Island by Grigor I. Shelikof (1*a*).

That fear of conquest was not the only reason why the natives objected to the landing of the Russians upon their shores is evident from the story related by an old native to Holmberg (1*b*). According to the story, the old and wise men of Kodiak objected to the landing of Glottof on the island in 1753 since, they said, "Who knows what sickness they may bring us?" Time proved that their fears were fully justified. It was inevitable that the contact with the Russians in 1741, with the Spaniards in 1775, with the English in 1776 and with the French in 1786 should lead to the introduction of diseases hitherto unknown among the natives.

Thus far little is known concerning the diseases which may have prevailed among the natives of Alaska prior to the coming of the white man. There is at present a paucity of data dealing with the paleopathology of the Alaskan natives. This may in part be due to the scarcity of material suitable for study resulting from the custom of the natives in disposing of their dead. Thus among the Eskimos the body placed in the fetal position was elevated several feet above the ground and exposed to the elements, while among the Tlingit cremation of their own dead and burial in the sea for their slaves were the methods usually employed. In addition there has been the usual wanton destruction by whites of skeletal remains which may have shown some pathological changes. Shelikof (2*a*), who in 1784 established a settlement on Kodiak Island, where he remained for two years, stated that he did not notice any epidemics of disease among the natives, that they did not know of smallpox and that they were of healthful habits and lived to be a hundred years old. On the other hand, Cook (3*a*) on his visit to Unalaska in 1778 commented on the fact that the natives did not seem to be long lived and that but few of them appeared to be above fifty years of age.

Much information regarding the traditions and customs of the natives, especially of the Aleuts, is found in the notes and letters of that keen observer Father Ivan Veniaminov (4*a*), who from 1824 to 1838 lived among the Aleuts

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and among the natives of Sitka. According to him the natives did not consider their medicine men as well trained as formerly. This, he was told, was due to the fact that prior to the coming of the white man the medicine men autopsied their slaves, in that way ascertaining the cause of death and learning how to improve their treatment. This practice, however, was discontinued with the coming of the white man; consequently the medicine men no longer understood the diseases as well and their treatment was not as efficient.

Despite the frequent occurrence of scurvy among the Russian explorers and among the early settlers, its absence among the natives is noteworthy. The Russians attributed the absence of scurvy among the natives to their use of dried berries and wild plants. That the natives suffered from some form of avitaminosis is suggested by the observations of La Pérouse (5), who explored the vicinity of Lituya Bay in 1786. He commented on the fact that they were feeble and that some suffered from swelling of the legs, although their gums were sound. Portlock (*6a*), while exploring in the vicinity of Cook Inlet in 1787, observed that during the winter months some of the natives suffered from swelling of the legs and sores, both of these disappearing with the coming of summer. Portlock attributes the improvement of these conditions to the use by the natives of the inner bark of some of the pine trees. From the description furnished by both La Pérouse and Portlock the occurrence of beriberi rather than scurvy is suggested.

Of the diseases introduced among the natives of Alaska none has produced such dire suffering and loss of life, nor reached such epidemic proportions and affected the economic and social structure of the country as did smallpox. It is to be recalled that Shelikof (*2a*), who came to Kodiak Island in 1784 and who spent two years among these natives, stated that they did not know of the smallpox. In the course of his explorations in Southeastern Alaska in 1787, Portlock (*6b*) observed that many of the adults bore scars from the smallpox. However, both he and members of his crew noted that children under the age of 10 or 12 years were free of such scars. Portlock also commented on the fact that while the Indians from the eastward who visited them while they were exploring in the vicinity of Cook Inlet were marked with this disease, those coming from the westward had no such signs. One of the old Indians informed him that the smallpox had visited them long ago and that it had killed many of the inhabitants. In view of the fact that the younger children had escaped the epidemic and that it was limited to the Indians of the east, Portlock concluded that it was in all probability introduced by the Spaniards who under Bodega and Maurelle came north along the Californian coast in 1775 to Mt. Edgecumbe. In 1795 two Aleuts who were with Zaikof were stricken with smallpox while in the vicinity of Yakutat Bay. In 1836, during the administration of Kuprianof, there occurred an epidemic of smallpox which, because of its high mortality, greatly influenced the economic and social status of the natives. This disease first appeared in the settlement of Tongass, where 250 of the 900 inhabitants succumbed. From here the disease spread to Sitka where, during a period of three months, 400 of the natives succumbed, while among the Russians there was reported but one case, which recovered. The mortality rate was especially high among the adults, and conspicuously less

so among the children and Creoles. As soon as navigation was opened the disease spread to Kodiak and to the coastal villages and from there into the interior. Village after village was depopulated and deserted, unburied corpses being left lying about. Kuprianof made vaccination compulsory wherever that was possible, and Dr. Blaschke vaccinated first the inhabitants of Sitka and then those of other parts of Alaska. It soon became evident that where vaccination was carried out the disease was brought under control, and the mortality rapidly dropped to 10 per cent or less, whereas in those areas, such as Cook Inlet, Prince William Sound and Bristol Bay, where the natives refused to be vaccinated, the mortality ranged from 40 to 60 per cent. Dr. Blaschke estimated that approximately 3000 natives died from smallpox before vaccination was introduced. The appearance of this disease in the various villages was definitely associated with the arrival of people from the infected areas, and it was not until 1840 that smallpox was brought under control in Alaska.

An interesting eyewitness account of the smallpox epidemic as it occurred in Sitka is given in detail by Father Veniaminov (7). He states that upon the appearance of this disease the natives attempted to infect with the smallpox virus the meat and fish sold to the Russians. Appeal was made to the Shamans to control the disease, and the air was filled with the sounds of drums, shouting and singing. Some of the more intelligent, realizing the ineffectiveness of this method of control, appealed to the Russians for help. It was then that Dr. Blaschke began to vaccinate the natives, and Father Veniaminov noted that among those vaccinated none developed this disease. News of the effectiveness of this treatment soon spread, and natives who formerly depended upon the Shamans for treatment now appeared and requested that they be vaccinated. Subsequently natives from the surrounding villages came in for this prophylactic treatment.

Since many of the able-bodied adults died during this epidemic, leaving behind, in great want, children and aged, the new Governor, Etolin, ordered the consolidation of 75 small villages into seven larger settlements so that in times of stress they could help one another.

In 1843 and 1844 (1*e*) smallpox again appeared, but, due to the fact that great numbers had been vaccinated, the disease did not spread and was soon brought under control. The importance and value of vaccination was so ingrained in the natives that after the purchase of Alaska by the United States, natives would occasionally ask why the government did not send out agents to vaccinate them as did the Russians (2*b*).

It is questionable whether syphilis existed among the natives of Alaska prior to the coming of the white man. Its introduction here is the stereotyped history of exploration, exploitation and the introduction by the white man of new diseases, especially venereal, among natives. Beginning with 1743 many hunters and traders came to Alaska, where they established themselves and compelled the men to hunt and bring back the pelts while they remained with the native women (1*j*). Under these conditions there can be little doubt that venereal diseases were spread throughout the villages.

That the Russians were acquainted with syphilis is suggested by Billings' (1*g*) statement that, while his expedition wintered in 1792 on the west side of Illiuliuk Bay, Unalaska, a party of

Russians and natives from Kodiak paid them a visit and requested that they be given tobacco, brandy and some remedies for syphilis. The latter they obtained from the surgeon of the expedition.

Cook (*3a*), who visited Unalaska in 1778, remarked that "The women of Unalaska encouraged men, with the result that their health suffered from a distemper that is not uncommon here." It is difficult to conclude whether the distemper he mentions was gonorrhea or syphilis. Cook commented further upon the fact that the natives were subject to cancer or a complaint like it which those whom it attacked were careful to conceal. One cannot conclude from this statement whether the lesions mentioned were syphilitic, tuberculous or nonspecific in nature.

Lisianski (*8a*), who came to Alaska in 1804 from the Sandwich Islands, spent a year visiting Kodiak and Sitka. He commented upon the fact that the Alaskan natives are subject to venereal disease, consumption, itch and ulcers, and that slight venereal taints were removed by decoctions. However, when the disease touched the nose each nostril and sometimes the gristle was pierced through. That Lisianski (*8b*) knew of syphilis and its mode of spread is evident from his report, in which he stated that while at the Sandwich Islands he would not permit his crew to visit with the native women, since he was afraid of introducing among them a certain disease which was very prevalent there and which left marks of its ravages upon the faces of some of the inhabitants.

Golovnin (*1h*), who in 1818 reported on the condition of the colonies, stated that in former times syphilis was general among the Aleuts but was uncommon at the time of his visit. It was brought, he stated, to Kodiak by crews, although the commanders had been enjoined to inspect their men. At Sitka the Russians contracted the disease from the natives, who in turn became infected from the crews of the foreign vessels. The natives considered this disease rather lightly and indifferently. In his discussion of the low birth-rate among the Aleuts, Father Veniaminov (*2c*) stated that one of the causes was the introduction by the Russians of various diseases which interfered with the fertility of the natives, but that this cause was not under control. He stated that syphilis was introduced by the Russians and committed its greatest ravages about 1798. At that time it was widespread and in some families all members bore marks of the disease.

Dall (*9a*), who explored the Yukon Territory in 1866, failed to mention syphilis as one of the diseases noted among the Indians of that area. He stated that zymotic diseases were unknown, but that the Indians did have various mild diseases of the skin, boils, small tumors and urethritis. With the transfer of Alaska to the United States and the arrival in Sitka of American troops, venereal disease spread rapidly, and within six months after their arrival nearly the whole Sitka tribe of 1200 natives was said to be infected (10). William G. Morris (11), in his report of the custom districts of Alaska, called attention to the prevalence of syphilis among the natives and the importation and spread of this disease by both troops and miners. He stated that syphilitic diseases were the greatest bane of the country, especially because, in 1877, at the time that this report was written there was not a physician in the whole of southeastern Alaska. Writing in 1880, Petroff (*2b*) stated that syphilis was probably first introduced by the Russians,

and at that time existed most commonly in coast settlements and in the interior where intercourse with the seaboard was maintained. It was found, he stated, in all stages, and remained untreated except at trading centers where physicians were stationed. Writing in 1933 of the Eskimos of the Kuskokwim, Hrdlicka (12) stated that syphilis is uncommon among the natives along this river.

There is no definite evidence at this time that tuberculosis among Alaska natives antedated the coming of the white man. If tuberculosis, either pulmonary, or in its extrapulmonary forms, such as lupus, scrofula or tuberculosis of bones and joints, had existed, some of the surgeons who accompanied the Russians on their explorations would have mentioned this fact since it would have been as widespread as it subsequently became. That the natives were susceptible to tuberculosis is evident by the fact that once this disease was introduced, it spread rapidly.

It is significant that not until 1770, or 29 years after the discovery of Alaska, do we find a record of the occurrence of tuberculosis among the natives. Berg (1*i*) reported the death from tuberculosis of two Aleuts who were in Siberia enroute to St. Petersburg.

It is of interest to learn that several of the Alaska explorers died from tuberculosis. Chirikoff (1*j*), who discovered Alaska in 1741, died from this disease in 1747. Cook (3*b*) reported the death of his surgeon in 1778 in Alaska from tuberculosis and Captain Charles Cook (9*b*), who succeeded Cook, died in Kamchatka in 1779 from tuberculosis.

It is evident that tuberculosis once introduced among the natives of Alaska spread rapidly, for Lisianski (1*e*), who visited Alaska in 1814, commented that tuberculosis was among the most common diseases noted among the natives. A more detailed account of the occurrence and character of tuberculosis was given by Father Veniaminov (4*b*), whose notes were very kindly translated for me by Father A. P. Kashevaroff, Curator of the Territorial Museum, Juneau, Alaska. Father Veniaminov not only commented upon the frequency of this disease among the Aleuts with whom he lived from 1824 to 1838, but described two forms of this disease. One form manifested itself by cough, expectoration, hemoptysis and dyspnea. This form of tuberculosis the natives considered as being incurable, while the second form, which Father Veniaminov termed "rotting from the kidneys," was frequently associated with loss of appetite, emaciation, and pain in the chest and was considered as curable or amenable to treatment. The treatment outlined by the natives for tuberculosis consisted of rest, starvation, decoction of various herbs and blood-letting in the region below the ribs.

Blaschke (13), who was in charge of the medical service at Sitka, reported that consumption and scrofula were both common among the natives of this region, while Romanowsky (14), in 1848, reported that phthisis was prevalent among the natives of the Aleutian Islands and especially among the mixed bloods. In his narrative published in 1847, Simpson (15) commented upon the fact that among the natives of Alaska hemoptysis was a common complaint. From the symptoms described by Dall (9*c*) as occurring in a 12 year old boy, it would seem that by 1870, if not earlier, tuberculosis occurred in the Yukon Territory. While Dall did not specifically report the occurrence of tuberculosis, the fact that he reported seeing cases of pleurisy, pneumonia and bronchitis is at least sug-

gestive that some of the diseases encountered may have been of tuberculous origin.

In his very exhaustive and authoritative report dealing with the population, industries and resources of Alaska, from the time of its discovery until 1880, Petroff (2*d*) concluded that the high morbidity and mortality from pulmonary diseases could be attributed to the insufficient clothing of the natives, sleeping in cold nooks and insufficient covering. The pulmonary diseases do not show any predilection for any special tribe or area of Alaska. One of the customs which may have favored the spread of tuberculosis in the early days was that of the devoted wives swallowing the expectoration of their sick husbands. Father Veniaminov (2*e*) mentioned that the Aleuts had a superstition that disease could be prevented by having their children swallow the viscid expectoration obtained from an old man famous for his achievements and his irreproachable character.

Petroff (2*d*) claimed that after consumption the largest number of deaths was to be attributed to scrofula. This disease manifested itself as malignant ulcerations with resulting large disfiguring scars. The natives were apathetic about the condition, which was aggravated by lack of care.

That tuberculosis is present in about one-third of the Eskimos of the Kuskokwim region is the conclusion drawn by Hrdlicka (12) in his report of 1933. He stated that it would seem that these natives have developed some degree of immunity, since this disease was more chronic in nature than formerly. In the adults the disease usually attacked the lungs, while among the children the disease manifested itself either as tuberculosis adenitis or lupus or tuberculosis of the bones or joints.

Fellows (16) has analyzed the causes of death during the five year period of 1926 to 1930 inclusive. He found the total death rate per 100,000 population during this period as 1846 for the native population and 1190 for the white population. The death rate from tuberculosis was 655 and 56 per 100,000 for the native and white population respectively. Among the natives tuberculosis was the cause of death in 35.5 per cent of cases, while among the white population tuberculosis was the cause of death in but 4.7 per cent. There is no doubt that tuberculosis has been and is at the present time the most common cause of death among the natives of Alaska.

It is improbable that cattle or milk played a rôle in the dissemination of tuberculosis among the natives of Alaska. It is true that as early as 1795 cattle had been imported from Siberia to Kodiak Island and to Unalaska (1*k*). However, these animals did not thrive and perished shortly thereafter. It is stated (1*k*) that in 1833 the Russian American Company had 220 head of cattle in Alaska, but that by 1883 the herd rarely exceeded 20 head. Because of the fact that the Alaskan natives were unaccustomed to the use of fresh milk, this never became a widely used item of food.

It must be evident that tuberculosis in both pulmonary and extrapulmonary forms is in the vast majority of instances of human rather than bovine origin, in view of the fact that there is no parallel between the distribution of cattle and the occurrence of this disease.

The occurrence in 1807 at Unalaska of an epidemic of bloody diarrhea which resulted in the death of large numbers of young people was mentioned by Father Veniaminov (2*c*). This disease made its appearance following the wreck of an American vessel and was alleged to be due in most instances to the eating of

wet rice. That the epidemic might have been cholera is suggested by the bloody stools, rapid spread of the disease and high mortality.

Petroff (2*d*) mentioned the occurrence of an epidemic of measles and of hemorrhagic measles which first appeared on Kodiak Island and the contiguous mainland.

Other diseases which have been reported by Petroff (2*d*) as occurring in epidemic proportion include "typhoid pneumonia," which has appeared from time to time, affecting especially the villages situated along the coast. Dall (9*c*) reported an epidemic of hysteria which resembled the religious mania observed in other places. This epidemic, which occurred in Nulato in 1867, was characterized by "fits," tearing of clothes, rolling on the ground, convulsions and the appearance of unconsciousness. Dall, realizing the hysterical nature of the condition, advised the use of birch twigs, which he stated soon put an end to the symptoms.

The remedies employed by the natives consisted of scarification, blood-letting, actual cautery, ligation, steam baths, fasting and the use of decoctions of various herbs and plants. In addition the Shamans treated the sick by exorcism, beating of drums, singing and dancing.

Lisianski (8*c*) described in detail the process of blood-letting as he saw it performed by a native woman. He stated that the vein was first transfixed with a stout needle held in a piece of wood, and that by means of a copper instrument, which was far from sharp, the overlying skin was cut until the blood gushed forth.

According to Dall (9*d*) it was customary among the natives of the Yukon to destroy the house and the belongings of those who died. In order to save the house the moribund patient was frequently placed outside of the house in a tent.

A hospital existed at St. Paul as early as 1808 (17). Simpson (15), in describing the hospital at Sitka which he visited in 1842, stated that it had 40 beds, and that a hospital with its appointments would not be a disgrace to England. In 1860 this hospital admitted 1400 patients, of whom but 22 died.

For many years the priests of the Russian Orthodox Greek Catholic Church of America have kept a register of the causes of death which have occurred in their parish. These records have been translated by the Rev. A. P. Kashevaroff, Curator of the Territorial Museum, Juneau, Alaska, and are on file at the office of the Territorial Auditor. From Kodiak Island and vicinity the causes of death have been recorded since 1825, from Cook Inlet and vicinity since 1846, from Afognak since 1896 and from Prince William Sound since 1897. In analyzing the reports from the various parishes one is impressed, on the one hand, by the large number of deaths attributed to tuberculosis, and, on the other hand, by the relatively small number of deaths attributed to other diseases of the pulmonary system. Among the recorded deaths which occurred in the Kodiak Island district, tuberculosis and pleurisy constituted the most common cause of death. In 1827 there were recorded several deaths due to syphilis, and from time to time carbuncles appear as the cause. In 1865 scarlet fever and in 1868 parotitis appear, while in 1875 there was a high mortality from measles. In 1881 and again in 1889 many deaths were attributed to "grippe."

Anemia is not uncommonly found as the cause of death among the Cook Island reports. Here, as in the reports from Kodiak Island, carbuncles are fre-

quently found as the cause of death. In 1875 the death of 51 people was reported in the village of Kustaten, from ptomain poisoning following the eating of a beluga whale.

Of 153 deaths reported from Prince William Sound during the years 1897 to 1916 inclusive, 54 were attributed to tuberculosis. Among the death records of Afognak, tuberculosis and scrofula are frequently given as the cause of death. Mumps and "cold" and, in 1913, measles occur as among the more common causes of death in this area.

Although little is known of the occurrence of diseases among the natives of Alaska prior to the coming of the white man, the reports and records of the early explorers lead us to conclude that diseases due to food deficiency did exist, that smallpox, syphilis and tuberculosis were unknown and were in all probability introduced by the white man. Smallpox, introduced probably by the Spaniards, caused more havoc than all of the other diseases. Syphilis brought in by the trappers, traders and especially by the sailors became widespread. Tuberculosis, while not occurring in the epidemic proportions of smallpox, has nevertheless taken a great toll of human lives since its probable introduction by the white man more than a century ago. The priests of the Russian Orthodox Church have contributed valuable information by recording in their parish registers the cause of death of their communicants. The translation of these records by Father Kasheveroff has made it possible to determine the nature of the various epidemics which from time to time occurred among the natives of Alaska.

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Paré's *Cinq Livres de Chirurgie:* Text and Translation of the Epistolary Dedication

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As a result, presumably, of one of those herd-like movements to which even historians and bibliographers occasionally succumb, Paré's *Cinq livres de chirurgie*, published at Paris in 1572, remained, as it were, "lost" in modern times, until Haberling, in 1928, published a description of it.[1] The bell-wether in this case must certainly have been Paré's most eminent disciple, Malgaigne, who never saw the book and who was able only to conjecture, and that not entirely accurately, its contents. Paré's most recent bibliographer, Miss Janet Doe, has, nevertheless, been able to establish the existence of copies in ten of the most important libraries in Europe, and another in private hands, as well as three copies in this country, one of these last being still privately owned.[2] A fifteenth copy, a recent happy acquisition[3] by the library of the College of Physicians of Philadelphia, furnishes the material for this communication.

"The *Cinq livres*," writes Miss Doe (p. 69), "contains all new material. It has been called by several serious writers Paré's *chef-d'oeuvre*. . . . To begin with [she is here quoting Haberling], in it appears the first description of the fracture of the head of the femur ([Paré], p. 94). Secondly, it is the first appearance of the whole teaching of bandages, fractures, and dislocations which has come down to us from the ancients, broadened by Paré's own experience. Lastly, we recognize here, as in no other book, the author's genial mode of presenting his material. . . . The text of the *Cinq livres* itself is greatly rearranged in the collected works."

Paré is an author cherished by historians and biographers, because he was himself, consciously or unconsciously, a historian and autobiographer. This characteristic appears throughout his work, and certainly in the epistolary dedication of his *Cinq livres*. Haberling has given two brief quotations from this "epistle"; some of its material on charlatans reappeared later, as Miss Doe points out, scattered through the "Introduction" to the *Oeuvres*, and thus found its way, via the Latin translation of the *Oeuvres*, into Thomas Johnson's linguistically delightful "Workes of . . . Ambrose Parey" (1634): but the entire original text can be found nowhere, I

[1] Wilhelm Haberling. Die *Cinq Livres de Chirurgie* des Ambroise Paré (1572). In: *Festschrift zur Feier seines 60. Geburtstages am 8. Dezember 1928 Max Neuburger*, Wien, 1928 (*Internationale Beiträge zur Geschichte der Medizin*). Haberling cites Haeser as being the first historian to have had the book in his hands, though his reference to it (1881) passed unnoticed by other writers on Paré. I owe the Haberling reference to Doe, *n.* 2, below.

[2] Janet Doe. A bibliography of the works of Ambroise Paré. Chicago, Univ. of Chicago press, 1937.

[3] An acquisition made possible largely through the generosity of Dr. Francis C. Grant and his fellow-members of the Philadelphia Academy of Surgery.

believe, but in the fifteen recorded copies. While the text contains, perhaps, nothing particularly new, it is Paré plain, and deserves, I believe, the reprinting accorded it here. And I believe that "those who do not understand the [French] tongue, whose number is infinitely large, will be grateful to [me] for this, that . . . [it is also] communicated to them in my mother language, in terms that they understand."[4]

[4] Paré's defensive arguments on this point (see below) are ironically countered by the fact that it was the Latin translation of his work, all of it originally written in French, that first established his universal importance for his time. Inasmuch as he constantly seeks to elevate the standards and the status of surgery by stressing the importance to the surgeon of a knowledge of anatomy, pharmacy, and nutrition, it might seem strange that he did not urge upon the *jeunes Chirurgiens* a knowledge of the scientific languages also. But this would have entailed a personally disadvantageous capitulation to the lordly and troublesome medical faculty, and one should perhaps not ask a surgeon under such circumstances to add quixoticism to his other, very real, virtues.

The French text has been reproduced literally, except that words abbreviated in the original have here been written out in full; in other words, a conscientious attempt has been made to reproduce any original errors and inconsistencies, and not to provide any second-hand ones. The translation is, doubtless, not delightful, linguistically or otherwise; insofar as differences in idiom permit, it is literal, or that was the intention. It is my belief that the literal translation is more likely than one which is *fardé* to catch some of the flavor of the original, and it is generally agreed that a literal version tends to be more accurate. But apologies are made in advance for the inaccuracies and inelegancies that will be found. There would be more of them, had I not been able to pick the Gallic ventricles of the brains of Mr. R. H. Baugh, the library's periodicals assistant, and two or three other friendly associates, to all of whom I am happy to acknowledge indebtedness.

Au Trespvissant et Tres-Chrestien Roy de France, Charles neufiéme de ce nom, Ambroise Paré, son premier Chirurgien, & tres-humble seruiteur.

S.

SIRE, la Chirurgie (selon le tesmoignage de Celse autheur tresgraue & excellent entre les medecins latins) outre ce qu'elle est la plus ancienne partie de la medecine, aussi est elle la plus certaine & necessaire. Car nous voyons plusieurs maladies guerir par le seul benefice de nature, sans l'ayde d'aucun medecin, ny obseruation de diete: tellement qu'on pourroit à bon droit douter, si la santé prouient par l'ayde du Medecin, ou bonté & force de nature. Mais quant

To the Most Powerful and Most Christian King of France, Charles, ninth of that name, Ambroise Paré, his chief Surgeon and very humble servant offers

Salutation.

SIRE, Surgery (according to the testimony of Celsus, an author of importance and excellence among the Latin physicians), besides being the most ancient part of medicine, is also the most evident and necessary. For we see several maladies healed by the sole benefice of nature, without the aid of any physician or dietary observance: so much so, that one could with good reason doubt whether health proceeds from the Physician's aid or from the kindness and power of

à l'operation manuelle, on n'en peut dire le semblable: car (afin que ie laisse plusieurs autres oeuures de Chirurgie non moins necessaires) comment seroit il possible de guerir vne fracture, ou luxation, sans la main du Chirurgien? En quoy ie ne me peux assez émerueiller de la miserable condition de ce temps, auquel les Chirurgiens, mesprisans ceste partie tant salutaire à la vie des hommes, l'ont laissée aux vulgaires & imposteurs, qui se nomment renoüeurs: comme prestres, moynes, artisans, charlatans, bourreaux, executeurs de haute iustice, ladres, femmes, & païsans des champs: lesquels font cent mille fois plus de mal que de bien, rendans les poures malades impotens, voire souuent leur ostans la vie: d'autant que telle maniere de gens ne sçauent aucunement l'architecture, ou composition de l'homme, qui s'acquiert par l'anatomie, laquelle est tresnecessaire, principalement aux fractures & luxations. Et si on me veut obiecter, & mettre en auant, qu'aucuns de ces renoüeurs se seroient trouuez par fois bons maistres: ie respondray, qu'en leur apprentissage ils ont fait, & font encores, plusieurs fois ouurir le ciel & la terre, par faute d'auoir puisé en cette fonteine Hippocratique & Galenique. Ne voit on pas combien & comment ils en font à croire? Car si on va vers eux pour quelque cheute, ou contusion seulement, iamais ces imposteurs ne sont despourueus de mensonge, disans qu'il y aura vn petit os hors de sa place, ou vn nerf tressailli, & autres semblables réueries. Et mesmes aucuns d'entreux sont si impudents, qu'ils se vantent que cette science de rehabiller, & renoüer, leur est acquise de race, c'est à dire, de pere en fils: qui est vne chose fort ridicule, & hors de toute raison: veu que l'homme naist sans sçauoir aucune chose: car s'il fust né auec quelque art, il n'eust

nature. But as regards manual performance, one can not say the same: for (leaving aside other, no less necessary works of Surgery) how would it be possible to heal a fracture, or dislocation, without the hand of the Surgeon? Wherefore I cannot wonder enough at the miserable condition of this day, in which the Surgeons, misapprehending this business, so beneficial to the life of men, have left it to the vulgar and the impostors who call themselves bone-setters; such as monks, priests, artisans, charlatans, hangmen, executioners, lepers, women, and peasants from the fields, who do a hundred thousand times more harm than good, reducing the poor sick to helplessness, often even taking away their life, inasmuch as this manner of people knows not at all the architecture or composition of man, which knowledge is acquired by anatomy, a very necessary art, especially for fractures and dislocations. And if one wants to object, and to put forward that some of these bone-setters would occasionally be found to be good masters, I reply that, in their apprenticeship-stage, they have cut open many times, and still do, heaven and earth, for want of having drawn upon this Hippocratic and Galenic spring.

Does one not see how much and in what manner they seek to inspire belief? For if one goes to them for some fall, or mere contusion, these impostors are never unprovided with a falsehood, saying that it's a matter of a bone being out of place or of a strained nerve, and other similar imaginings. And some of them are even so impudent as to boast that this science of restoration or bone-setting was acquired by them through blood, that is, from father to son—which is completely ridiculous and beyond all reason, seeing that man is born having no knowledge whatever: if he had been

iamais voulu apprendre les autres. Il est vray, que Dieu a donné à chacun des autres animaux quelque chose de particulier, & de naturel, dés leur premiere essence, ce qu'il n'a fait à l'homme[5]. *Comme pour exemple: le coq chante les heures de nuit, & de iour, plus certaines que nul horologe: la mouche à miel bastit ses rayons, ou alueoles: la formi prepare & acomode ses greniers, ou elle entre par des labyrinthes, ou chemins tortus: l'araigne tist & file sa toille: l'arondelle & autres oyseaux font leurs nids d'vn artifice admirable: autres pronostiquent le temps aduenir, à sçauoir s'il y aura vent, pluye, tempeste, disette de biens, ou fertilité: les autres sçauent se medeciner, & autres choses, qui sont impossibles à déchiffrer par le menu. Aussi ne sçauroient ils faire autre chose, que ce qui leur a esté donné pour leur naturel, & ce de certaine origine à nous incogneüe. Mais en lieu que l'homme naist dépourueu d'art, il est doüé de raison: & son ame immortelle (qui est vn rayon de la divinité) peut apprendre tous arts & sciences. Donc de vouloir croire, que le fils d'vn bon Chirurgien peut estre Chirurgien, si premierement il n'a esté instruit: ce seroit chose aussi peu vray-semblable, que le fils d'vn gentilhomme, lequel sçauroit bien picquer & voltiger vn cheual, & courir la bague, peust faire comme son pere, si premierement il n'auoit monte plusieurs fois à cheual, & qu'on ne luy eust monstré ceste industrie. Partant ce seroit vne chose trop temeraire, de vouloir aneantir l'authorité de tant d'hommes doctes & illustres fondée en raison & experience, pour suiure l'opinion vulgaire des choses fausses & mensongeres: laquelle nonobstant est si enracinée, non seulement au cerueau du*

[5] Paré later elaborated these ideas on the natural habits of animals, as Haberling and Doe point out, in his *Livre des animaux & de l'excellence de l'homme*, first issued in the second edition (1579) of the *Oeuvres*.

born with knowledge of some art, he would never have been inclined to learn the others. It is true that God has given to each of the other animals some native peculiarity—along with their primary essence—but He did not do the same for man.[5] For example, the rooster calls out the hours of the night and day more reliably than any clock; the honey-bee constructs its comb or cells; the ant prepares and puts together its store-houses, which it enters by labyrinths or tortuous ways; the spider weaves and spins its web; the swallow and other birds build their nests with an admirable skill; some foretell the weather, to wit, whether there will be wind, rain, storms, a dearth of produce, or fertility; others know how to heal themselves and other things impossible to unravel in all their particulars. Furthermore, they would not know how to do anything but what is given them as their natural endowment, and that from a certain origin unknown to us. But whereas man is born unprovided with any art, he is endowed with reason; and his immortal soul (which is a ray of divinity) is able to learn all arts and sciences.

Thus, to be willing to believe that a son of a good Surgeon can be a Surgeon without first having undergone instruction,—this would be as little likely as that the son of a gentleman, who knew well how to spur and vault on his horse and engage in a tilting match, could do as his father did if he had not first been on a horse a number of times and been shown this skill. Consequently, it would be a temerarious matter to wish to annihilate the authority, founded on reason and experience, of so many learned and illustrious men, to follow the vulgar opinion in matters that are false and illusory. This opinion, nevertheless, is so deeply rooted, not only in the brain

simple populaire, mais aussi en l'esprit de plusieurs gens estimez doctes, qu'à grand peine elle semble pouuoir estre ostée: combien que i'espere, qu'apres qu'on aura leu & entendu les raisons desquelles i'vse en ce petit liure, tel erreur demeurera nul. Or (SIRE) *afin que me complaignant de tels abuseurs ie ne semble alleguer cecy trop legerement, ie vous prie, n'y a il pas à Lyon, à Dijon, & en plusieurs autres villes de vostre Royaume, des femmes qui se disent renoüeuses? Mesmes en vostre ville de Thoulouse, il n'y a pour le iourd'huy que le bourreau qui soit appelé pour reduire les os rompus, & luxez: comme en la ville de Pamiers en Faiz, & à Mons en Hainaut, en la ville de Heidelberg en Allemagne: & qui voudroit en faire la recherche, on en trouueroit bien d'auantage. Que diray ie plus? En vostre ville de Morlaiz en Bretaigne, les ladres (qu'ils appellent Caquins) ne sont ils pas seuls qui reduisent les os? Quant aux autres, ils sont semez en toutes pars. Donc (comme i'ay cy dessus dit) n'est-ce point vne extréme & deplorable infelicité en ce siecle, de veoir les Chirurgiens delaissans cest oeuure tant excellent, & necessaire, entre les mains de telle maniere de gens, qui n'ont intelligence ne certitude de ce qu'ils font? Qu'il soit vray, si on leur baille les os nuds d'vne anatomie seiche, ils ne sçauroient bien les remettre en leur places. Comment seroit il donc possible, estans couuers de chair, qu'ils le puissent faire? Mais ie sçay la response des Chirurgiens. C'est, que quand ils auroient bien reduit vne luxation, ou fracture, le peuple abbruué de long temps de ces abuseurs, n'y auroit aucune fiance, & les appelleroit tousiours: lesquels estans appelez, pour se monstrer*

of the simple common people, but also in the mind of many people commonly regarded as learned, that it seems to be able to be removed only with great difficulty; how much do I hope that, after my arguments in this little book have been read and understood, such error will no longer remain!

Now (SIRE), in order that, complaining of these abuses, I may not seem to make these allegations too lightly, are there not, I beg you, at Lyon, at Dijon, and in several other cities of your realm, women who call themselves bone-setters? Even in your city of Toulouse there is today only the executioner who can be called to set broken bones and dislocations; as is the case in the city of Pamiers in Foix, and at Mons in Hainaut, in the city of Heidelberg in Germany; whoever wishes to undertake the search will find many more similar instances. What more shall I say? In your city of Morlaix in Brittainy, are not the lepers (whom they call *Caquins*) the only ones who set bones? As for the others, they are scattered everywhere.

Thus, (as I have said above) is it not an extreme and deplorable infelicity in this age, to see Surgeons abandoning this work, so excellent and necessary, to the hands of people of this sort, who have no apprehension or certainty of what they are doing? Let it be granted that, if one hands them the bare bones of a dry anatomy, they would not know how to put them back in their places. How is it possible, then, that they could do it when the bones are covered with flesh? But I know the Surgeons' reply. It is that, when they have done a good reduction of a dislocation or fracture, the people, long worn down by these deceivers, have no confidence and continue to call on the bone-setters. These, having been called in, in order to show

bons maistres, feront à croire, que l'os ne sera bien reduit, & contemneront l'oeuure du Chirurgien rationel: qui fait qu'ils s'en sont deportez. Veritablement les magistrats des villes, amateurs des lettres, d'honneur, & de vertu, deuroient leur deffendre telles oeuures, attendu que pour vne partie fracturée, ou luxée, qui ne sera bien reduite, le malade demeurera impotent, & miserable toute sa vie. Il y a encores vne autre maniere de gens beaucoup plus fascheuse, importune, & pernicieuse: lesquels cognoissans que les oeuures susdites ne se peuuent faire sans douleur, toute-fois taschent à abuser le poure peuple, affermans qu'ils pourront remettre les os fracturez & luxez, par certaines paroles, moyennant qu'ils ayent le nom & la ceinture du malade. Mais ie m'émerueille, comment il est possible aux hommes, qui ont entendement (ou le doiuent auoir) de croire vne mensonge si aperte, veu que la loy sacrée des Medecins anciens, principalement du diuin Hippocrates, dit, que pour reduire les os fracturez, & luxez, il faut tenir, tirer, & pousser: pour laquelle chose les anciens ont inuenté vne infinité de machines & instrumens, lors que par force des mains on ne peut assez suffisamment tirer les membres pour faire la reduction. Et ces imposteurs veulent persuader, qu'ils feront par paroles ce que la main & les machines ne peuuent quelquefois faire. Ie laisse maintenant à declarer la deüe situation des parties, les compresses, astelles, & ligatures, desquelles on s'ayde pour faire tenir les os fracturez, & luxez, iusques à ce que le callus soit fait, & les ligamens affermis. Ie laisse aussi les bandages, desquels aucuns seruent à cette intention, les autres à exprimer le sang loing de la partie offensée, & le repousser vers les autres parties du corps,

themselves good masters, pretend that the bone has not been well set and speak disparagingly of the work of the rational Surgeon, who does what they desist from doing. Truly, the magistrates of the cities, lovers of letters, of honor, of virtue, ought to forbid them such works, considering that through a fractured or dislocated part which is not well reset, the invalid will remain helpless and miserable all his life.

There is still another manner of person, much more unpleasant, importunate, and pernicious; these, knowing that the above-mentioned operations cannot be performed without pain, nevertheless attempt to abuse the poor people, asserting that they could reset the fractured or dislocated bones, through certain words, on condition that they have the name and the girdle of the patient. But I marvel how it is possible for men who have any sense (or ought to have) to believe so flagrant a deception, seeing that the sacred law of the ancient Physicians, principally that of the divine Hippocrates, says that, to reduce fractured and dislocated bones, it is necessary to take fast hold, pull and push; for which the ancients invented an infinite number of machines and instruments, inasmuch as by force of hand one cannot pull the members sufficiently to effect the reduction. And these impostors would like to persuade us that they do by words what the hand and machines are sometimes unable to do. I forbear mentioning the proper placement of the parts, the compresses, splints, and ligatures, which one uses to hold the fractured and dislocated bones until the skin is hardened and the ligaments made strong. I omit also the bandages, of which some serve this purpose, others to press the blood far from the offended part and push it to the other parts of the body, for

de peur que par sa trop grande abondance il ne cause inflammation, aposteme, & autres grans accidens. Ie laisse semblablement les medicamens, lesquels il conuient changer selon le temps de la maladie: aussi la maniere de viure, laquelle faut diuersifier selon l'aage, coustume, temperature du malade, & saison de l'année: toutes lesquelles choses ne se peuuent faire ny accomplir par paroles. Or (SIRE) *ie vous supplie ne croire iamais cela, que premierement ne l'ayez veu. Car quant à moy, il m'est tellement incroyable, qu'encores que ie le veisse de mes yeux, si croirois-ie plustost que ce seroit vne vraye magie et imposture. Et ou telle chose se pourroit faire sans fraude ny fallace, veritablement ie desireroye pour l'amour, le seruice, & ma vie, que ie dois à vostre Maiesté, que iamais vostre court ne fust sans quelqu'un de ses nouueaux Chirurgiens de paroles. Mais ie ne cognois aucun Chirurgien rationel en vostre Royaume, qui pour reduire vne fracture, ou luxation, n'afferme qu'il faille tenir, tirer, & pousser les parties luxées, ou fracturées, ainsi que nous auons declaré: & ne peut on faire telles choses sans grande douleur: ainsi que quand on couppe vn bras, ou vne iambe: ou quand on incise la chair, pour decouurir l'os du crane, afin de trepaner: aussi quand on applique fers ardens: ou que l'on extrait vn enfant mort hors le ventre de la mere (lequel sera ia fort enflé, & commencé à pourrir) pour l'extraction duquel il conuient mettre la main, & quelquefois certains instrumens, ou quand on fait autres oeuures grandes & serieuses, toutefois necessaires pour sauuer la vie des hommes. Mais faut il pour cela appeler les Chirurgiens cruels & inhumains, & les auoir en horreur? ou leur faire ainsi que le peuple Romain feit iadis à Archa-*

fear lest too great an abundance of it may cause inflammation, an abscess and other serious incidents. I omit, similarly, the medicaments, which it is meet to change according to the stage of the illness; also, the mode of living, which must be varied according to the age, custom, temperature of the invalid, and the season of the year; all of which things can not be done or accomplished by words.

Now (SIRE) I beg you never to believe that which you have not first seen. As for myself, it is unbelievable that what I have seen with my own eyes I should believe, nevertheless, rather to be true magic and delusion. And if such a thing could be done without fraud and deception, truly I would desire, out of the love, service, and my life, that I owe to Your Majesty, that your court never be without one of these new Word-Surgeons. But I know no rational Surgeon in your kingdom who, to reduce a fracture or dislocation, does not affirm that it is necessary to hold fast, pull, and push the dislocated or fractured parts, as we have declared: and these things cannot be done without great pain; as when one amputates an arm or a leg; or when one incises the flesh to uncover the bone of the cranium, in order to trepan; as when one applies the hot iron; or when one extracts a dead infant from the belly of the mother (which will be greatly distended and have begun to putrify), for the extraction of which it is fitting to use the hand and sometimes certain instruments; or when one performs other important and serious operations, necessary, however, in the saving of human lives.

But is it necessary therefor to call the Surgeons cruel and inhuman, and to hold them in horror? Or to do to them as the Roman people did of old to Archa-

buto[6], *l'vn des premiers Chirurgiens que les Romains receurent en leur Republique, lequel (ainsi que Sextus Cheronée nepueu de Plutarque raconte) pour-ce qu'il coupoit bras, & iambes, & faisoit autres oeuures, appartenantes à son art, fut en telle horreur à la commune de Rome, qu'il fut tiré hors de sa maison, & lapidé au champ de Mars? ô quelle ingratitude! auoir employé tout son bien, esprit, & temps pour apprendre son art, & en l'exerçant estre ainsi massacré & tué! Or iaçoit que le peuple semblast auoir quelque couleur en ce fait, si est-ce qu'il ne fut aduoüé du Senat: qui ne pouuant autrement reparer vne si grande faute, & mécognoissance de ce populace (le plus souuent furieux & inconsideré en ses faits) pour recognoitre les seruices & perfections d'iceluy, luy feit ériger pour perpetuelle memoire vne statuë d'or, qui fut posée au temple d'Esculapius. Quant à moy donc* (SIRE) *ie suis de l'aduis de Celse, qui admoneste le Chirurgien, d'estre asseuré en ses oeuures, & non piteux, ou craintif: en sorte, que quand il opere de sa main, il ne soit aucunement émeu pour la clameur du malade, ny des assistans: & que pour cela il ne se haste point plus qu'il ne faut, ny aussi qu'il ne retarde plus qu'il n'est besoin: mais qu'il acomplisse son intention, sans auoir égard aux cris & au dire de ceux, qui par leur ignorance méprisent le Chirurgien. Et considerant, que pour les choses susdites cette tant noble partie de Chirurgie a esté dés longtemps delaissée, & mal entenduë, laquelle toute-fois est plus requise que les autres, pour diuers inconueniens, ausquels les hommes sont subiets: voyant mesmes* (SIRE) *le danger auquel vous estes iournellement obiecté, courant à cheual par vne trop*

[6] This curious misprint for *Archagathus* was corrected when this early surgeon was similarly referred to in the "Introduction . . . à la chirurgie" which opens the collected works.

buto[6], one of the first Surgeons whom the Romans received in their Republic? He (as Sextus Chaeronaeus, nephew of Plutarch tells), because he cut off arms and legs and performed other operations belonging to his craft, was held in such horror by the commune that he was dragged out of his house and stoned in the Field of Mars. What ingratitude! To have employed all his means, intelligence, and time in learning his craft, and while practicing it, to be thus massacred and killed! Now, although the people seemed to have some show of justification for this act, nevertheless, it was not approved by the Senate, which, being unable to repair so great an injury and such ingratitude on the part of this populace (very often headlong and thoughtless in its actions), in order to recognize his services and perfections, caused to be erected in perpetual memory of him a statue of gold, which was placed in the Temple of Aesculapius.

As for myself then (SIRE), I am of the opinion of Celsus, who admonishes the Surgeon to be resolute while operating, and neither pitying or fearful; to the point that, when he is operating with his hand, he be entirely unmoved by the cries of the patient, or those of the watchers; and that these influence him neither to hasten his work more than he ought, nor retard it more than there is need to; and that he carry out his intention without regard to the cries and words of those who because of their ignorance despise the Surgeon. And having in mind that, for the things mentioned above, this so noble branch of Surgery has for a long time been abandoned, and ill understood, which nevertheless is more needed than others for divers mischances to which men are subject; seeing also (SIRE) the danger to which you are daily subjected, riding

grande vitesse, tant à la chasse, à la lice, qu'ailleurs, qui pourroit estre cause vous rompre, ou denoüer quelque partie de vostre corps, ou de messieurs voz freres, Princes, & autres nobles Seigueurs, qui suiuent vostre Maiesté, (dont ie prie Dieu qu'il vous vueille garder) ie me suis efforcé d'en faire ce petit traité, pour me refraichir la memoire, que le temps emporte auec soy, redigeant par écrit, ce que i'ay cogneu estre vtile & expedient pour les accidens susdits. Aussi pour le desir que i'ay de non celer vn tel bien à la Republique, ie l'ay bien voulu mettre en lumiere, n'ignorant point toute-fois, qu'Hippocrates, Galien, & autres excellens personnages ont doctement traité de cette matiere: & encore n'agueres M. Iacques d'Alechamps, docteur en medecine, demeurant en vostre ville de Lion: auquel les Chirurgiens sont grandement tenus, pour l'interpretation de plusieurs liures des anciens qu'il a mis en nostre langue Françoise, pour l'intelligence des ieunes Chirurgiens: apres lesquels ie ne mets la main à la plume, pour en mieux écrire: mais seulement ie m'efforce d'exposer plus clairement ce, qui peut auoir esté par eux assez obscurément ou confusément écrit. Car d'autant que la methode d'Hippocrates est briéue, elle est volontiers acompagnée d'obscurité: & les commentaires de Galien sont fort prolixes, & sa doctrine semée & entrelacée ça & la, selon les passages qu'il a voulu expliquer: ce qui peut engendrer grande confusion au ieune Chirurgien: ioint que le temps, & vsage, ont apporté depuis beaucoup de choses necessaires à la cure des maladies: qui est cause, que i'ay trauaillé à reduire par ordre, le plus familierement que il m'a esté possible, ce que i'en ay compris tant par leurs liures, que par l'experience, que i'en ay fait depuis le temps que Dieu m'a appelé à ceste vocation. Et à ce

your horse too rapidly to the chase or the lists or elsewhere, which could be the cause of breaking or dislocating some part of your body, or those of the Princes, your brothers, and other noble Lords who follow your Majesty, (from which I pray that God may protect you), I have striven to compose this little book to refresh my memory, which time carries off with itself, committing to writing what I have learned is useful and expedient for the accidents mentioned above. Also because of my desire not to keep secret from the Republic so great a boon, I have been willing to print it, being not unaware, however, that Hippocrates, Galen, and other excellent personages have treated learnedly of this matter; and again, but lately, M. Jacques Dalechamps, doctor of medicine, residing in your city of Lyon, to whom Surgeons are greatly bound for the interpretation of several books of the ancients which he has put into our French language for the understanding of young Surgeons. After these I do not take my pen in hand to write better, but merely to attempt to set forth more clearly what may have been written by them somewhat obscurely or confusedly. For, although the method of Hippocrates is one of brevity, it is readily attended by obscurity, while the commentaries of Galen are very prolix, and his doctrine is scattered and interwoven here and there according to the passages which he wished to explain—which is capable of causing great confusion for the young Surgeon. Add to this that time and experience have since brought many necessary things to the cure of the sick; which is the reason I have labored to reduce to order, in as homely a manner as I could, what I have learned from their books as well as from my own experience since the time when God called me to this

ay inseré plusieurs figures & pourtraits, partie pris des anciens, & partie de mon inuention, qui mettent deuant les yeux, comme le Chirurgien y doit proceder, ainsi qu'en la chose mesme. Dauantage il m'a semblé bon d'écrire vn autre petit traité de la piqueure & morsure des bestes venimeuses, & de celle des chiens enragez: auquel on trouuera remedes bien approuuez, voire plus certains que d'enuoyer en la mer, ou autre part, ceux qui en sont mords. Car ils ont esté inuentez des anciens auec grande raison, & les ay maintefois experimentez auec bonne & certaine yssuë, sans iamais en auoir veu aduenir aucun mauuais accident.

Le surplus de ce present traité est vn recueil de certains remedes contre la goute, lesquels en partie i'ay pris des liures des anciens, & en partie inuentez de moy-mesme par coniecture metodique, & que i'ay aussi souuentefois experimentez & pratiquez. Mesmement en vostre suitte au voyage de Bayonne[7]*, par toute les villes ou ie passoye, ie me suis tousiours enquis aux gouteux, de quels remedes ils vsoient pour appaiser leurs douleurs: & ayant recueilly ce que chacun d'iceux y faisoit particulierement, & conduit par methode rationelle, ie l'ay bien voulu exposer en public. Or cette matiere des goutes n'est pour vous* (SIRE) *mais elle pourra seruir aux gouteux, qui ne vous peuuent suiure à la chasse: lesquels, lors qu'ils auront leurs douleurs, desireront à veoir & tenir ce liure, auquel ie m'asseure qu'ils prendront plaisir, pour la diuersité des remedes qu'ils y trouueront, dont ils pourront estre aydez à seder & appaiser leurs tourmens. Et prie Dieu* (SIRE) *que d'icy à quatre vingts ans vous y puissiez aussi prendre*

vocation. And to this end I have inserted a number of figures and pictures, partly taken from the ancients, in part of my own invention, which place before the eyes how the young Surgeon ought to proceed, even as in the acts themselves. More, it seemed to me well to write another little treatise on the sting and bite of venomous beasts, and of that of mad dogs, for which one will find well-approved remedies, even more certain than that of sending into the sea or elsewhere those who have been bitten. For these were invented by the ancients with good cause, and I have experimented with them many times with good and evident issue, without ever having seen any bad accident befall.

The remainder of this present treatise is a collection of remedies against the gout, which in part I have taken from the books of the ancients, in part invented myself by methodical conjecture, and which I have often experimented with and used in practice. Likewise, in your suite on the journey to Bayonne[7], in all the villages through which I passed I invariably inquired of the gouty what remedies they used to allay their pains; and having collected what each of them did in particular, and guided by a rational method, I wished to publish them. Now, this subject of gout is not for you (SIRE), but it may serve the gouty, who cannot follow you to the chase. When their pains shall have come upon them, they will wish to see and hold this book, in which I am sure they will take pleasure for the diversity of remedies which they will find and by which they will be aided in quieting and assuaging their torments. And pray God (SIRE) that from now to 80 years you also may be able to take

[7] Paré devotes a brief passage in the *Apologie et traicté contenant les voyages* (first printed in the *Oeuvres* of 1585) to the journey to Bayonne, which consumed two years, 1564–6, but does not recall therein that it provided him with material for his book on the gouts.

recreation. Mais pource que ce pendant il pourra seruir aux ieunes Chirurgiens, ie me suis fort estudié à me faire entendre à iceux, ce que ie procure en tous mes écrits: car c'est à eux que ces pieces se rapportent, & non pas aux doctes, lesquels ie reuere & honore vniquement: qui est cause, que i'ay vsé de langage familier, & non fardé, sçachant bien que leur but & intention est, plustost d'apprendre la methode de bien curer, que de parler élegamment: car le parler ne guerist pas les malades (comme dit Galien) mais l'oeuure de main, & les remedes deuëment appliquez. Nonobstant ie ne l'ay pas voulu publier, sans le monstrer à plusieurs medecins & Chirurgiens bien experimentez, qui l'ont approuué, & entre autres, à Maistre Robert Greaume[8]*, Docteur Regent en la faculté de Medecine en ceste ville de Paris, lequel est grandement exercité & versé en icelle science, & és bonnes lettres Grecques & Latines, qui par ma priere a paracheué de donner des noms Grecs aux goutes des iointures, ausquelles les anciens n'en auoient point imposé. Car nous n'auons iusques icy que Chiragra, Ischias, Gonagra, & Podagra: combien que les goutes peuuent occuper toutes les iointures: pour laquelle cause il leur a doctement approprié noms conuenables, selon les autres iointures ausquelles ceste maladie peut aduenir*[9]*. Outre ce, l'ay bien voulu communiquer à Maistre Raphael de Tailleuis, Medecin du defunct Roy de Nauarre, non moins docte que bien experimenté en la medecine & Chirurgie, qui a souffert plusieurs années ceste maladie arthritique: lequel a aussi approuué mon labeur. Or* (SIRE) *ayant cogneu le con-*

[8] Robert Greaume and Raphael de Taillevis are mentioned by Paré, in the dedicatory epistle of his *La méthode curatiue des playes* (1561–2), as having performed a similar service for that book, the former having also furnished the Greek terms used therein (Doe, p. 52).

[9] Haberling (p. 155) cites as being among these

recreation herein. But, meanwhile, that it may be of service to the young Surgeons, I have applied myself hard to the task of making them understand what I provide in all my writings; for it is to them that these pieces relate, and not to the learned, whom I revere and honor without reserve. That is the reason that I have used the familiar language, unadorned, knowing well that their end and intention is rather to learn the method of curing well than to speak elegantly: for (as Galen says) the sick are not healed by words, but by the work of the hand and remedies duly applied.

Nevertheless, I did not wish to publish this without showing it to several highly experienced physicians and Surgeons, who have approved it, and among others, to Master Robert Greaume[8], Doctor Regent in the faculty of Medicine in this city of Paris, who is widely practiced and versed in this science and in the Greek and Latin literature. At my request he has finished giving Greek names to the gouts of the joints on which the ancients imposed none. For up to now we have only Chiragra, Ischias, Gonagra, and Podagra, although the gouts can occupy all the joints. Therefore he has learnedly adapted suitable names to them, corresponding to the other joints in which this malady may occur[9]. Beyond that, I wished to communicate it to Master Raphael de Taillevis, Physician of the deceased King of Navarre, no less learned than well experienced in medicine & Surgery, who suffered from this arthritic malady for several years; he also approved my labor.

Now (SIRE), having known the satis-

neologisms the following: Siagonagra (gout of the jaw); Trachelagra (gout of the neck); Rachisagra (gout of the vertebral column).

tentement qu'auez eu en receuant humainement, & prenant plaisir à reuoir plusieurs fois les dix liures de la Chirurgie que ie vous ay dediez, auec le Magasin & figures des instrumens necessaires aux Chirurgiens, cela m'a donné de rechef hardiesse enuers vostre Maiesté, de luy consacrer & presenter auec toute humilité encore ceux-cy: lesquels si ie cognois vous estre agreables, ie m'efforceray (s'il plaist à Dieu) de mettre bien tost en lumiere autre oeuure de la mesme profession, pour le desir que i'ay de profiter au bien public, & à la posterité. Et suis asseuré, que ceux qui n'entendent la langue Latine, desquels le nombre est innumerablement grand, vous sçauront bon gré de ce, que soubs vostre Maiesté ces presens liures leurs sont communiquez en mon langage maternel, & intelligible. Car la Chirurgie ne consiste seulement en speculation & intelligence, mais principalement en action, & en mettant la main à l'oeuure. Dieu vueille qu'ainsi soit, comme ie espere: auquel ie supplie,

SIRE, *qu'il vous vueille donner longues années, lignée, & prosperité en ce monde, & en fin felicité perpetuelle.*

faction that you have had in accepting graciously, and in pleasurably re-examining several times, the ten books of Surgery which I dedicated to you, with the magazine and figures of instruments needed by Surgeons, this has given me once more the boldness towards your Majesty to consecrate to him and present with all humility these books also; and if I learn that they prove agreeable to you, I shall strive (if it please God) to publish soon another work of the same profession, out of my desire to be of service to the public good and to posterity. And I am sure that those who do not understand the Latin tongue, whose number is infinitely large, will be grateful to you for this, that under your Majesty, these present books are communicated to them in my mother language, in terms that they understand. For Surgery consists not only in speculation and intellect, but chiefly in action, and in putting the hand to the work. May God will that it be as I hope; whom I entreat,

Sire, to ordain that you be given length of years, progeny, & prosperity in this world, & finally, felicity everlasting.

Memoir of Henry Khunrath Pancoast, M.D.*

By Eugene P. Pendergrass, M.D.

DR. HENRY K. PANCOAST was born in Philadelphia, February 26, 1875, and died at his home in Merion, May 20, 1939, after a short illness, at the age of 64. The immediate cause of death was a coronary thrombosis, but prior to this Dr. Pancoast had been ailing for several years from hypertension, during which time he had had several cerebral attacks (hemiplegia), each of which had taken its toll.

Dr. Pancoast's parents belonged to the Society of Friends and from them he inherited the characteristics so often noticed in those of Quaker ancestry—an absolute "level headedness" and common sense, which in him were augmented by a kindliness of nature that endeared him to his friends.

His father, Seth Pancoast(1823–1889), also a physician, and a graduate of the University of Pennsylvania, was a descendant of one of the three Pancoast brothers who came to Philadelphia with William Penn. In 1853 Seth Pancoast was made professor of anatomy in the Woman's Medical College of Pennsylvania. Later he was appointed professor of anatomy in the Pennsylvania Medical College (now nonexistent). Seth Pancoast contributed considerably to medical literature, (several books), and in this work he was assisted tremendously by his wife, Susan Osborn Pancoast (Dr. H. K. Pancoast's mother), who was a literary scholar and who did extensive translations from Greek, Latin and German. One of Seth Pancoast's later books, "Blue and Red Light, or Light and its Rays in Medicine," published in 1877, was of interest in the preparation of this memoir, in view of the discussion of *rays*, electricity, magnetism, and the effect of filters in the use of the various wave lengths of light in the cure of disease. It would seem that Dr. Henry K. Pancoast's interest in the physics of radiation was a result of his heredity or early environment.

Henry K. Pancoast obtained his entire preliminary education at Friends Central School, Philadelphia, graduating at the head of his class in 1892. From his early boyhood it was known that he desired to study medicine; but the loss of both of his parents before his graduation from Friends Central made it necessary for him to work several years before entering medicine. During this period he was employed at the Centennial Bank in West Philadelphia at 32nd and Market Streets. Dr. Pancoast often remarked, in his later life, that this training was invaluable.

In 1894, Henry K. Pancoast entered the Medical School of the University of Pennsylvania and graduated in 1898. His records in Pennsylvania were extraordinary, and he was selected therefore for interneship in the Hospital of the University of Pennsylvania, along with such men as Drs. Anspach, Biggs, Carnett and Norris.

After the completion of his interneship in 1900, Dr. Pancoast was appointed to the surgical staff of Dr. J. William White, and from 1901–1904 he served as an assistant instructor in clinical surgery and assistant demonstrator in surgery

* Read January 3, 1940.

in the Medical School of the University of Pennsylvania. It was during this period that Dr. Pancoast developed an interest in radiology, the stimulation probably growing out of a vision of its applicability to surgery.

The earliest history available indicates that the first x-ray department in the United States was established by the University of Pennsylvania, in 1896. Dr. Charles Lester Leonard was made the director of the department and had the title of "Skiagrapher." The department consisted of one room on one of the upper floors of the William Pepper Clinical Laboratory, in which there was housed a 7-inch Queen coil, operated by 20-volt storage cells, with a current broken by a mechanical spring interrupter. In 1897, the department was moved to a room in the Surgical Dispensary, in the then new Agnew Memorial Pavilion. The x-ray room, 10 x 20 feet, was partitioned off from the waiting room of the old Surgical Dispensary. The "dark room" was located two floors above, under the old surgical amphitheater. Dr. Leonard, in his hospital report in 1900, commented upon the increased and extensive use of the x-ray department in diagnosis and therapeusis, and reported a total of 86 patient-examinations for the year. It would have required the vision of a clairvoyant to visualize present demands on the department, which are in excess of 10,000 patients a year. Dr. Leonard resigned in 1902 and Dr. Pancoast was appointed "Skiagrapher" to succeed him. In training for his new work, it was necessary for Dr. Pancoast to spend eight to ten hours (total time) with Dr. Goodspeed, professor of physics at the University of Pennsylvania. At the expiration of this training period, Dr. Goodspeed told Dr. Pancoast that he had taught him all he knew of the subject, and that any further knowledge would have to be gained through experience.

During the next five years, the demand upon the x-ray department grew, and it was therefore necessary to move to larger quarters and obtain more modern equipment. It was during this period that Dr. Pancoast made his first contribution to medical literature, and, by unceasing labor and unselfish devotion to his work, developed an x-ray department that was attracting attention in other schools of medicine. In 1912, Dr. Pancoast was elevated from skiagrapher to professor of roentgenology. The University of Pennsylvania was the first medical school in the United States to establish such an exalted teaching position for this young branch of science. Subsequently, Dr. Pancoast's title was changed to professor of radiology, to conform with the recommendations of the American Medical Association.

Several Philadelphia radiologists, physicians and electrical engineers were responsible for many of the developments in roentgenology that occurred in the early days and, inasmuch as Dr. Pancoast took such an important part, it would seem appropriate to mention a few of the developments briefly. It is well known to many of the older Fellows of the college that both Drs. Leonard and Kassabian were martyrs to the development of medical radiology, and their experiences had a profound influence upon their colleagues in Philadelphia and elsewhere. Dr. Leonard's hands were badly burned at the time that Dr. Pancoast succeeded him in 1902.

During Dr. Pancoast's early experiences, an 18 inch coil with a mechanical interrupter was used to produce x-rays. In a personal letter, Dr. H. Clyde Snook, who invented the x-ray transformer and

is now a consultant to the Bell Telephone Laboratories in New York, says that early in 1902 Dr. Pancoast was regarded as unusual and as a pioneer in spirit and practice. Dr. Snook relates an experience that he had with Dr. Pancoast at that time that demonstrates how the latter was searching for better tools with which he could work. Dr. Snook received an urgent call from Dr. Pancoast to fix his induction coils. After first aid had been given to the coil, and it was operating again, Dr. Snook says that Dr. Pancoast was dissatisfied with the outfit and asked Dr. Snook questions such as: "Is there a coil anywhere in the world that will work better? Is there anything better?" Dr. Snook hesitatingly told him, no. Then Dr. Pancoast stated that he felt as if it were unwise to continue in this new field, as too much effort was required to get results that were not dependable. It was at that time that Dr. Snook revealed to Dr. Pancoast his secret, which was that he (Dr. Snook) was working on a transformer that he thought would assist greatly in the production of x-rays. And it was to Dr. Snook that Dr. Pancoast later loaned his "pet x-ray tube" (all of the gas tubes of that vintage were unstable) to try out on the new invention, the x-ray transformer; unfortunately, when the current was turned on, the tube blew up. Tubes, then, as now, were a limiting factor.

Many unusual experiences were encountered in the early efforts of performing a roentgen examination. Dr. Pancoast used to tell of a man who was referred for a roentgen examination of the spine. At that time, it required an exposure of approximately ten minutes to obtain a single plate of the spine. As this particular patient was in bed, and the bed would not go through the door into the x-ray room, the annunciator wire had to be strung from the coil, in the far end of the room, to the tube in the hall. The wire was supported by bandages hung to the chandelier. The tube was one of the old Queen variety, with the terminals on the outside, affixed by sealing wax. The tube was clamped into a burette holder and placed on a wide board, and inserted under the patient's back. During the exposure, a spark from the wire jumped to the head of the bed, the heated sealing wax permitted the terminal of the tube to come off and the wire dropped on the patient. The cracking sparks, hitting the patient from all directions, were too much for him. He jumped out of bed, ran down stairs, got his clothes, and left the hospital, preferring to take chances on being hit by another trolley car rather than go through the experience of a roentgen examination.

In 1903, the American Roentgen Ray Society held its annual meeting in Philadelphia, in Houston Hall at the University of Pennsylvania. At that meeting Dr. Pancoast made his first report of 100 cases of malignancy treated by x-rays. One of the reported cases concerned a young negro with extensive lupus vulgaris of the face, eyelids and nose, who had been referred for treatment from the ophthalmological clinic. The x-ray treatment had destroyed the pigment, so that the healed skin was white. An enterprising newspaper reporter made a photograph of the patient and obtained one of Dr. Pancoast, and these two photographs appeared side by side in an evening newspaper, captioned, "The doctor responsible for turning a negro white by x-ray treatment." Thereafter Dr. Pancoast received congratulatory letters from all over the world; there were even a humorous rhyme in "London

Punch" and some offers of membership in learned societies. Subsequently, a negro woman brought in her daughter, to have her made white, feeling that the daughter's chance in life would be enhanced. A letter from South America inquired as to the charge for a box of x-rays to turn a black man white. The negro with lupus vulgaris referred to above is still seen from time to time, and he is always willing to chat about his experiences in side shows.

It would seem appropriate in a memoir such as this to discuss briefly the various influences (developed in Philadelphia) that led to some of the advances in diagnosis and therapy. Possibly one of the main ones was the Philadelphia Roentgen Ray Society, organized by Drs. Leonard, Pfahler, Shober, Goodspeed, Pancoast, and possibly a few others, in 1905. These pioneers used to meet in each other's offices, at frequent intervals, and discuss mutual problems. It was during this period that Dr. Pfahler popularized the use of x-ray filters, Dr. Clyde Snook learned the necessity for the x-ray transformer, Dr. H. Threlkelv-Edwards developed his intensifying screens, Dr. William Sweet invented his foreign-body eye-localizer, and, a few years later, Dr. David Bowen described his new developing tank. All of these discoveries and inventions exerted exceedingly prominent influences upon radiology elsewhere. As a result of these inventions it was realized very soon that Philadelphia should make an effort to provide post-graduate instruction in the new science. The Philadelphia Post-Graduate School of Roentgenology which was then formed was the first of its kind in the United States and it remained in existence until 1915. The teachers included Drs. Pancoast, Pfahler, Manges, Bowen, Newcomet and Snook.

The constructive influences of Dr. Pancoast on the evolution of radiology were potent. He published well over one hundred papers, two monographs, and was a contributor to several books. Some of his papers brought him international fame.

Very early in his career he became interested in the effect of radiation in the treatment of Hodgkin's disease and the leukemias. His publication on this subject in 1906 is still regarded as a masterpiece. One of his early patients included an assistant, a full-time pupil-nurse, who suffered considerable epilation as a result of too close contact with some of the patients during treatment. This young lady, five years later, developed splenomyelogenous leukemia and died from it. This case of leukemia, as well as those occurring in some of the early radiologists and technicians, served to direct attention to the possibility that irradiation was a causal factor in leukemia and led to the institution of greater protection for the operator.

Two of Dr. Pancoast's more important contributions are his works on the "Healthy Chest," done for the National Tuberculosis Association, and his collective studies on pneumonoconiosis and silicosis. This interest in the latter subject was manifest throughout his entire life, and he was recognized as the authority on the roentgen aspects of that disease.

After Dr. Charles H. Frazier became professor of surgery at the University of Pennsylvania, Dr. Pancoast did considerable work and wrote many articles on the roentgen diagnosis of intracranial lesions.

It would seem that, in the press of such

investigative activity, Dr. Pancoast could scarcely have found opportunity for additional occupations pursuant to his profession, yet he lost no opportunity to exercise his life-long interest in the progress of his colleagues. He became affiliated with the American Roentgen Ray Society in 1903, and was elected its president in 1912. In the field of radium therapy, the record of Henry Pancoast holds equal prominence as an example of the highest ideals of its practice. He was one of the charter members of the American Radium Society and became its president in 1919.

The opportunity for war service appealed to Dr. Pancoast's patriotic spirit. In the early days of the war, he was in the Army, connected with the unit of the Hospital of the University of Pennsylvania, and, during a short time, taught field radiology to many surgeons and radiologists who were assigned to the University Hospital. Much to Dr. Pancoast's disappointment, the University would not allow him to go with the unit to France, asserting that his services were required at the hospital. Thus Dr. Pancoast resigned from the Army and joined the Navy, receiving a commission as an assistant surgeon, with the rank of lieutenant, junior grade. Dr. Pancoast acted as a consultant to the Naval Hospitals at League Island and Gray's Ferry Road. He did much during his service to improve the radiologic departments in the various Naval hospitals not only in Philadelphia but elsewhere. He was likewise a consultant and adviser to the Naval officers in charge of the development of radiology on "Hospital Ships." Dr. Pancoast was never happier than during the period when he developed improved facilities for the service men. He was retired in 1919 to the inactive list with the rank of lieutenant.

Dr. Pancoast was one of a group who arranged for the creation of a Section on Radiology in the American Medical Association and served as its chairman in 1932. He served for four years as a Chancellor of the American College of Radiology, and did a great deal to crystallize the activities of that organization. On September 25, 1933, Dr. Pancoast was elected to the presidential chair of the first American Congress of Radiology. This was a spontaneous recognition of his long and fruitful life of service to radiology.

For years, Dr. Pancoast had talked about and read many papers stressing the value of higher standards in radiology. A committee of which he was a member ultimately succeeded in the establishment of the Board of Radiology, and he was elected its first president on Septemtember 28, 1933. Unfortunately, it was shortly after this that Dr. Pancoast had his first hemiplegic attack, and he was never able to engage actively in the deliberations of the Board after the first year of its existence. In a few years he was made Honorary President and held that title until his death.

Dr. Pancoast, after his marriage, became a presbyterian, and, in spite of his many activities, never allowed his work to crowd out his church activities. He was a regular attendant at church each Sunday, served as treasurer of the Tabernacle Church at 37th and Chestnut Streets for many years until he transferred his membership to the Ardmore Presbyterian Church. In the latter, he was soon elected an Elder and he served in that capacity until his death.

In concluding this memoir, I would like to quote Percy Brown, who has

beautifully described Harry Pancoast as a man. "He was a great radiologist. He was a man whose intellectual honesty was such that he despised mental side stepping, and ignored collateral subterfuge. His love for the truth was intense. To him it was a precious treasure, hopefully to be sought in every human heart. If at times he failed in his quest, he was unutterably chagrined; any attempt to suppress truth or distort it incurred his complete disdain.

"As time passes, many will arise to fill his place in the vineyard of Science wherein he labored, but in the final estimation, any man who can properly be classified with Henry Pancoast shall be happy indeed."

Memoir of Charles Prevost Grayson, M.D.*

By George M. Coates, M.D.

DR. CHARLES PREVOST GRAYSON, an active fellow of the College of Physicians of Philadelphia since 1904, died in the Hospital of the University of Pennsylvania, after an illness of several months, on August 16, 1939. He was in his eightieth year and still active in his profession and in his other interests and recreations, but he had outlived most of his contemporary professional colleagues and friends, and at his funeral, which took place on a stormy Saturday in the midsummer vacation time, there was but one professional friend of his own age present, Dr. Thomas Rundle Neilson, who was so soon to follow him.

Dr. Grayson came of good old distinguished American stock and he himself was a patriotic American, with high ideals of loyalty and devotion to his country. His father was Frederick William Spence Grayson, of Bardstown, Kentucky, the son of Capt. Alfred Grayson, United States Navy, lawyer and journalist, and of Eliza Coulter, of Baltimore, Maryland. His mother was Mary Mallet Prevost, of Philadelphia, daughter of General Andrew M. Prevost and Mary Coulter, also of Baltimore. His father was of an old Virginia family—his mother of a Huguenot family who founded Frenchtown, N. J. His brother is Mr. Clifford P. Grayson, the distinguished artist, whose pictures hang in the foremost galleries in this country.

Dr. Grayson was born October 15, 1859, at 1604 Spruce St. in Philadelphia and resided in West Philadelphia and at 262 S. 15*th* St. throughout his long life. He was educated here and graduated from the old Central High School in 1878, after having received early scholastic training in private schools, including Colonel Saunder's Military Academy. Many men who later became prominent in the social, professional, business and political life of the city received their secondary school instruction at old "Central High," which has an imposing list of prominent alumni, both past and present. Following his graduation from school, his inclination was to become a purser on a ship but, this falling through, he entered Jefferson Medical College in the fall of 1878 and graduated March 13, 1880 after the two year course in medicine which was customary at that time. Not satisfied with this, however, he entered the School of Medicine of the University of Pennsylvania and obtained an additional M.D. from that institution in 1881, his preceptor having been Dr. Grayson Mallet Prevost.

Following graduation, and while awaiting an appointment to a hospital internship (it was called a residency in those days), and rather expecting to go in this capacity to Blockley—now called more properly the Philadelphia General Hospital—he signed as a ship's surgeon on the S. S. Zeeland of the Red Star Line, running between Antwerp and New York, but when the ship was laid up in Antwerp, he was transferred to the Nederland which began her passage back to New York on November 19,

* Read January 3, 1940.

1881. On the return voyage, the Nederland encountered a terrific gale and the following passages are quoted from his account of this trip.

"November 25—Blowing too hard and too much for Stabeck (the ship's surgeon) to get around so the Capt. asked me to take his place. Went around with the old man and saw the sick. Awfully crowded and filthy dirty. November 26—Gale increasing and the sea tremendous. Waves falling on the deck like so many tons of iron. Wheel house almost completely demolished. Boats beginning to suffer and new lashings put over them. Spent an anxious night but slept well. November 27—A wild gale blowing and the sea terrific in its height and power. The boats were smashed one by one. Into the steerage with the Capt. The ship 'laying to' in the trough of the sea with her wheel lashed and engine motionless. Just after dinner, while I was in the Dr.'s room, an immense breaker struck us, carrying away the Chart House, the remaining boats, breaking the Bosun's leg, and injuring a lot of other sailors. Ran forward to the saloon and found everything in confusion, men and women shrieking and crying, water pouring in the skylight, lights out and everybody scared to death. Rather uneasy myself, but kept quiet and wore a cheerful countenance. The hole in the deck soon planked over and we managed to gradually quiet the men and women. To my room and found the glass port broken and everything in the room soaked. In the evening Stabeck and I set and splinted the Bosun's thigh. Ship lay to all night and the sea gradually went down. Slept with all my clothes on, on my wet bed."

The Nederland arrived in New York on December 12, 1881 and there is some evidence to show that Dr. Grayson saw further service as a ship's surgeon, but the record is incomplete. At any rate, he was resident physician (where he is listed as Charles Mallet Prevost Grayson) at the Pennsylvania Hospital for sixteen months in 1883 and 1884 and then became connected with various medical institutions in Philadelphia, such as the Charity Hospital, the Pennsylvania Hospital, the Philadelphia Hospital, the Philadelphia Polyclinic and College for Graduates in Medicine and the Hospital of the University of Pennsylvania.

In the Spring of 1881, we find Dr. Grayson attending the clinic of Dr. Dulles at the Presbyterian Hospital, in 1885 doing eye examinations at the Wills Eye Hospital, in February 1885 assisting Dr. Ralph Seiss at the Polyclinic Hospital, which seems to have been the beginning of his interest in otolaryngology and where he soon became first assistant in the ear dispensary. Having now decided to study the diseases of the nose, throat and ear, he became associated with Dr. Charles Burnett, one of the outstanding otologists in America, and Dr. Carl Seiler, who held a similar position in American laryngology.

He was on the staff of the Charity Hospital in 1885, where he notes that his work was "much hampered by a want of bandages and proper dressings". Three months of the summer of 1885 were spent with Dr. William H. Bennett at the Children's Seashore Home and Mercer House at Atlantic City. He soon after became physician to the Educational Home, the Presbyterian Home and the Old Man's Home, and during this period he reported clinical lectures at the Pennsylvania Hospital.

Gradually, as his interest and work in otolaryngology increased, he dropped many of these appointments and found time to study his specialty in Vienna,

Berlin and Paris. His record in the School of Medicine of the University of Pennsylvania is as follows: Assistant Physician in Dispensary for Diseases of the Throat, 1890–94; Attending Physician in Dispensary for Diseases of the Throat, 1894–95; Lecturer and Instructor in Laryngology, 1895–1903; Chief Physician in Dispensary for Diseases of the Throat & Nose, 1894–1905; Clinical Professor of Laryngology and Rhinology, 1903–1905; Professor of Laryngology, 1905–1926; Emeritus Professor of Laryngology, 1926–39. He was also laryngologist to the Philadelphia Hospital.

As a lecturer and clinical teacher, Dr. Grayson was always popular with his students, who held him in affectionate regard. His clinical course in the University Hospital was an elective but always filled, while his lectures were well attended and enjoyed. He had a fine speaking voice, a good practical arrangement of his subject, and conversational delivery, well illustrated with details from his own experience. Old students will remember especially his lecture on the voice, singing as well as speaking, where he demonstrated the wrong and the right way of vocalization by singing, without accompaniment, a verse of "Oh Promise Me" from De Koven's light opera "Robin Hood," then at the height of its popularity. Years after his retirement, it was the writer's privilege to have Dr. Grayson give to the third year class practically the same lecture, brought up to date by comments on current popular singers, Richard Crooks, Lawrence Tibbett, Lily Pons, John Charles Thomas, Nelson Eddy and others with whose work he was entirely familiar, but he resisted all efforts to induce him to again illustrate by singing. Indeed a great deal of his time was spent in the study of the voice and its culture. He possessed a fine baritone voice with excellent resonance and power and had taken lessons in his younger days from some of Philadelphia's most noted singing instructors. In addition to his love of singing, he had a thorough understanding of instrumental music and could perform with credit on the piano and guitar. He was a member of several amateur singing societies and, early in his career, took leading parts in amateur dramatic performances. This interest in music, the opera and the stage continued with him through his life and he was recognized as a connoisseur in these fields and it was this that enabled him to be of great professional assistance to many noted singers, as well as struggling beginners who had attracted his attention, through his understanding of and familiarity with their art, and he had a wide acquaintance among them. He had a catholic taste in literature, and was a scholarly and careful, although not a prolific, writer. A glance at his bibliography shows which branch of his work attracted him most, his best productions having dealt with voice physiology, voice culture, and the training and care of the voice. He belonged to the conservative school of otolaryngologists, and in the controversy which raged during the first decade of the present century concerning the relative merits of tonsillotomy and tonsillectomy, he was almost the last American of prominence to defend the former technic, although in England the question was not removed from debate for another twenty years.

From his youth, Dr. Grayson enjoyed drawing and painting, as might be expected in the brother of such an eminent artist as Mr. Clifford P. Grayson, but until his retirement from teaching he had little time to devote to this hobby. Immediately after retirement,

however, he enrolled as a student in the Life Class at the School of Industrial Art and continued to develop this talent until his last year.

Dr. Grayson never married but had a wide circle of acquaintances among the intellectual and social groups of Philadelphia, where he was always a welcome companion because of his varied interests, his delightful, friendly conversational powers, his buoyant, happy nature and his attractive personality. He was a handsome man, always well groomed and with exceptional good manners. With his fondness for society, the arts and sport, it was natural that he was a popular addition to his circles of friends in various walks of life, from the mercantile ship's coterie to his professional groups. He made many lasting friendships from boyhood onward with those who remained in the city to become outstanding in business and the professions, and with those who travelled in the service of their country. Among his intimates were high ranking officers in the United States Army whom he had known and visited with since cadet days at West Point. He had a great sense of loyalty and patriotism and was one of those early commissioned in the Officers Reserve Corps, and great was his disappointment when, after many and repeated efforts, he was unable, on account of his age, to secure an assignment to active duty during the World War. He served on the examining board in Philadelphia.

Dr. Grayson's interests, aside from those connected with his profession, were not confined to music and the drama. He was a sports' enthusiast all of his life, and, in his youth, a versatile performer. Swimming was his first choice perhaps, but he was almost as fond of baseball, cricket, tennis, sparring and horseback riding. He also enjoyed sailing, in the days when one could take a boat up or down the Delaware River, and he followed this form of recreation at the New Jersey, Rhode Island and Maine summer colonies during vacation time.

Dr. Grayson was a member of some of the most important medical societies pertaining to otolaryngology. In addition to the County and State Societies and the American Medical Association, he became a member of the College of Physicians of Philadelphia in 1904, of the American Laryngological, Rhinological and Otological Society in 1896 and of the American Laryngological Association in 1905. He also held membership in the Philadelphia Pediatric Society and the Pathological Society of Philadelphia.

In 1902 Dr. Grayson published his book entitled "The Diseases of the Nose, Throat and Ear," and in 1898 he was editor of the American edition of Grünwald's "Atlas and Abstract of the Diseases of the Larynx," and author of the sections on diseases of the throat and nose in *Progressive Medicine* in 1904 and 1905.

He was a member of the University, Rittenhouse, Racquet, Art and St. Anthony's Clubs, the Historical Society of Pennsylvania, The Sons of the American Revolution, and a Major in the Medical Section of the Officers Reserve Corps. In politics he was a Republican.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

Regular Meeting, January 22, 1940

A Comparison of the Prothrombin Levels of Maternal and Cord Blood at Delivery. Robert F. Norris, M.D., and Alexander Rush*, M.D. (*Abstract 1, below.*)

An Evaluation of Circulation Time in the Diagnosis of Peripheral Vascular Disease. J. Edward Berk*, M.D. (*Abstract 2, below.*)

The Treatment of Malignant Tumors of the Testicle. George W. Chamberlin, M.D., and John H. Jamison*, M.D. (*Abstract 3, below.*)

The Use of Synthetic Substances Having Vitamin K Activity in the Prevention of the Hemorrhagic Tendency of the Jaundiced Patient. Jonathan Rhoads*, M.D. (*Abstract 4, below.*)

Regular Meeting, February 26, 1940

The Clinical Application of Histone Zinc Insulin and Globin Insulin to the Treatment of Diabetes Mellitus. Garfield G. Duncan, M.D., and Charles A. Barnes*, M.D. (*Abstract 5, below.*)

Eosinophilia and Pneumonitis in Chronic Brucellosis. Kendall A. Elsom, M.D., and Franz J. Ingelfinger*, M.D. (*Abstract 6, below.*)

Observations upon the Effect of Coramine in Certain Cardiac States. William D. Stroud, M.D., and Paul H. Twaddle*, M.D. (*Abstract 7, below.*)

The Relation of Diet to the Protection of the Liver from Injury. Samuel Goldschmidt*, Ph.D., Harry M. Vars*, Ph.D., and I. S. Ravdin, M.D. (*Abstract 8, below.*)

Abstracts

1. A Comparison of the Prothrombin Levels of Maternal and Cord Blood at Delivery. Robert F. Norris, M.D., and Alexander Rush, M.D.

The average prothrombin values of 50 mothers and 51 babies at delivery by the Quick test were found to be above normal in the mothers and below normal in the babies. Repetition of the tests 7 to 14 days after delivery in 32 mothers and 33 babies showed no significant change in the prothrombin values of the mothers and only a slight increase in those of the babies. The average volume of packed erythrocytes was much greater in the case of 39 babies than in their respective mothers. The discrepancy between the prothrombin values of mother and child must, therefore, be proportionately larger for whole blood than for plasmas. The Quick test is thought to be a reliable clinical procedure, but sources of error in the method are discussed. It is suggested that comparison of the 25 per cent dilutions of unknown and control plasmas gives more reliable determinations than comparison of the undiluted plasmas.

2. An Evaluation of Circulation Time in the Diagnosis of Peripheral Vascular Disease. J. Edward Berk, M.D.

* *By invitation.*

* *By invitation.*

Through the intravenous injection of 5 cc. of 10% magnesium sulphate solution the normal circulation times from the arm to the hands and from the arms to the feet were determined from 405 complete tests upon 200 normal individuals. These were compared with the times obtained in a group of 21 proven cases of peripheral vascular disease, upon whom 83 complete tests were performed.

Individuals with peripheral vascular disease exhibited a distinct tendency toward a longer circulation time and a definite increase in the number of "blank" and "persistent blank" reactions. This same tendency was also seen in the arm to tongue circulation times when the results from 340 tests on 166 normal individuals were compared with those from 74 tests in the same 21 cases of proven peripheral vascular disease.

Wide variations in circulation times were obtained both in the normal and the abnormal groups even within the same individual. The possible reasons for this were discussed.

The possible explanations for the prolonged circulation time and the greater number of "blank" reactions in peripheral vascular disease were discussed.

The test was felt to be of some value in the diagnosis of peripheral vascular disease but had the great disadvantage of being a completely subjective determination.

3. The Treatment of Malignant Tumors of the Testicle. George W. Chamberlin, M.D., and John H. Jamison, M.D.

Incidence: Testicular tumors occur in about 1% of all patients as malignant. *Age:* Thirty-two of our forty-five patients were between the ages of twenty and forty. *Histology:* 17 were teratoma; 11 were sarcoma; 6 were embryoma; 2 were mixed tumors; 2 were carcinoma. *Symptoms of the Primary Tumor:* Thirty-two had painless swelling; in five trauma was noted; seven had pain, and in four there were no symptoms of primary tumor. *Symptoms of Metastatic Involvement:* Pain in the back and indigestion were the most common complaints. Constipation or diarrhea occurred in some patients. Cough, pain in the chest, and enlargement of the super clavicular lymph nodes indicated metastasis above the diaphragm.

Preoperative Diagnosis. It is sometimes difficult. It depends upon the history and physical examination, hormone tests, roentgenographic examination and therapeutic trial of irradiation. The last of these is probably the most reliable. An intravenous urogram often indicates metastasis of the retro peritoneal lymph nodes before there is any other clinical evidence of metastasis. Displacement of the kidney in any direction or displacement or obstruction of the ureter are signs of great importance. The excretion of prolan in the urine was not a reliable test in our series. In many instances where a radio sensitive tumor was present, the prolan figures were low. In only two patients with embryonal tumor was the prolan excretion greater than five hundred mouse units by the Ferguson technique.

Treatment. We have divided our forty-five patients into three groups. First, those who received radiation therapy to the lymphatics and to the tumor and then had an orchidectomy. Second, those who were treated after orchidectomy and third, those who were first seen with evident metastasis. In group one, there were twelve patients of whom nine or 75% are living and well, one and one-half years or more. In group two, there were sixteen patients

of whom nine or 56% are living and well, one and one-half years or more. Of the combined groups one and two, there were twenty-eight patients of whom eleven or 39% are living and well, five years or more. There were seventeen patients in group three, of whom three are now living and well, an average of ten years.

An ideal type of treatment to be applied to a patient with a malignant testicular tumor may be outlined as follows: Early diagnosis by the history and physical examination, roentgen examination and prolan study, and intravenous urogram to determine the relations of the upper urinary tracts. Roentgen examination of the chest. Intensity of radiation over the lymphatics in the abdomen and primary tumor. Orchidectomy in four to six weeks. If the tumor is radio sensitive, radiation should then be given over the chest and neck. If the tumor has been radio resistant, no further radiation should be given.

4. The Use of Synthetic Substances Having Vitamin K Activity in the Prevention of the Hemorrhagic Tendency of the Jaundiced Patient. Jonathan Rhoads, M.D.

During the past year Vitamin K has been shown to occupy a unique place among the vitamins in that its biological activity is shared by certain chemically related synthetic compounds, some of which are actually more potent than the pure crystalline vitamin prepared from natural sources.

Of these the most important is 2 - methyl - 1,4 - naphthoquinone. Other important synthetic substances with vitamin K activity are Phthiocol, 4-amino-2-methyl naphthol hydrochloride, and the dihydroxy-, dibutyric- and dipropionic-derivatives of 2-methyl-1,4-naphthoquinone.

2-methyl-1,4-naphthoquinone has been used orally with bile salts in 23 patients with prothrombin deficiency. In 16 of these patients the prothrombin concentration returned to normal. In 4 some improvement occurred and in 3 the prothrombin concentration fell in spite of treatment. The minimal effective dose used was 1 milligram, the maximum dose given was 120 milligrams over a period of 5 weeks. The maximum dose in one day was 30 milligrams by mouth and 12 milligrams by rectum.

This material is unsuitable for subcutaneous or intramuscular administration. The dibutyric derivative has been used intramuscularly but the response was slow. The dipropionic derivative has been used by mouth in five patients but proved to be less effective than the unconjugated 2 - methyl - 1,4 - naphthoquinone.

For intravenous use 4-amino-2-methyl naphthol hydrochloride or a 1 to 10,000 solution of 2-methyl-1,4-naphthoquinone in physiological saline solution is suitable. The dihydroxy-derivative can also be used. It is somewhat unstable. We have used each of the first two compounds in five patients with hypoprothrombinemia. 3 milligrams was the minimum effective dose with the 2-methyl compound and it appears that slightly larger doses will be required with the 4-amino derivative.

No toxic effects have been observed and the toxicity of these compounds according to animal experiments performed elsewhere appears to be far below the therapeutic dose.

Three patients who failed to respond to the 2-methyl-1,4-naphthoquinone came to autopsy. Histologic examination of the liver in each case showed

such marked degenerative changes that it is postulated that the fall in the prothrombin level observed corresponds to the progressive fall in prothrombin concentration observed in the completely hepatectomized dog.

5. The Clinical Application of Histone Zinc Insulin and Globin Insulin to the Treatment of Diabetes Mellitus. Garfield G. Duncan, M.D., and Charles A. Barnes, M.D.

Histone Zinc Insulin is a suspension of a mixture of histone and insulin, with zinc added in the proportion of 0.2 mgm. to each one hundred units of insulin.

After a suitable control period each of ten adult patients with diabetes mellitus was given a single injection of Histone Zinc Insulin. Under conditions of continuous carbohydrate intake the level of the blood sugar was observed until the action of the insulin had ceased. The curves of the blood sugar levels thus obtained were compared with those from single injections of equal quantities of Protamine Zinc Insulin, and of either Unmodified or Crystalline Insulin. The action of Histone Zinc Insulin began immediately after injection and was maintained for eighteen to twenty-two hours. The effect of Protamine Zinc Insulin was delayed for six to eight hours and then continued for over twenty-eight hours. The action of Unmodified Insulin or Crystalline Insulin began immediately, reaching its height in four to six hours, and ending soon thereafter.

The immediate effect makes it unnecessary to add a quick-acting insulin to Histone Zinc Insulin as is so often necessary with Protamine Zinc Insulin. This was borne out by further studies in which a patient, after being controlled on a combination of Protamine Zinc Insulin and Unmodified Insulin, was transferred to a single injection of Histone Zinc Insulin. The type of curve of the blood sugar level with the Histone Zinc Insulin was similar to that obtained with the combination.

Preliminary studies indicate that Globin Insulin—a clear combination of Globin and Insulin—also has an immediate yet prolonged action.

6. Eosinophilia and Pneumonitis in Chronic Brucellosis: A Report of Two Cases. Kendall A. Elsom, M.D., and Franz J. Ingelfinger, M.D.

Two cases were described in which the outstanding features were extensive pneumonic infiltration, eosinophilia and immune reaction to Br. Abortus. The striking similarity of the clinical manifestations suggested a common etiology rather than a fortuitous association of symptoms. The clinical picture was thought to be a manifestation of chronic brucellosis.

The lung lesion in both cases consisted of a bilateral, diffuse, exudative pneumonitis which was recurrent in one instance, continuous in the other. It did not resemble pulmonary tuberculosis from a roentgenological standpoint.

In both cases the total leukocyte count varied between 10,000 and 15,000, of which over 40 per cent were eosinophiles. The eosinophilia ultimately disappeared.

In both instances the diagnosis of brucellosis rested on positive agglutination tests (1:400, 1:200), opsonophagocytic indices and skin tests.

Alternative diagnoses of Loeffler's syndrome, Hodgkin's disease, peri-arthritis nodosa and trichinosis were considered and rejected.

7. Observations upon the Effect of Coramine in Certain Cardiac States. William D. Stroud, M.D., and Paul H. Twaddle, M.D.

Although there is convincing evidence of the efficacy of Coramine (Ciba) in the cerebral and respiratory depression of drug poisoning (barbiturates, etc.), there is little data concerning its effect on the heart or on the respiratory distress of heart disease.

The purpose of this study was to observe its effects on patients with cardiovascular disease, emphasizing particularly its action in cases with respiratory distress. Nine patients, with either Cheyne-Stokes respirations or paroxysmal attacks of dyspnea, were given Coramine in doses of 3 to 4 cc. repeated four or five times daily, in most instances orally, and on the whole obtained marked relief within one to three days. Little constant change was noted from prolonged oral use in 6 cases with moderate heart failure, on the vital capacity, blood circulation time, electrocardiogram, blood pressure, pulse rate or in increase in urinary output. Intrathecal pressure fell between 22 to 95 mm. of spinal fluid in all of seven instances following intravenous doses of 5 cc., with the maximum fall reached in ten to twenty minutes. Venous pressure similarly fell in seven out of nine trials, but to a lesser degree.

It has been demonstrated that Coramine has a beneficial action on the abnormal respirations associated with cardiac disease. Dramatic responses, however, are not usually found from oral doses, but rather a slow progressive improvement,—usually one to three days elapse before the optimum benefit is realized. A more prompt but transient response follows its use intravenously and may be attended (as used in 5 cc. doses) by symptoms from widespread cerebral stimulation. Cardiac efficiency was not shown to be constantly improved from prolonged oral use. Decline in intrathecal pressure, following its intravenous administration, was observed and, to a less constant or striking degree, a decline in venous pressure. That these pressure changes are directly related to the improvement noted is considered doubtful. The present evidence points to its stimulation, as a chemical agent, of the respiratory receptors, either peripherally or centrally.

8. The Relation of Diet to the Protection of the Liver from Injury. Samuel Goldschmidt, Ph.D., Harry M. Vars, Ph.D., and I. S. Ravdin, M.D.

Diets rich in carbohydrate or protein decrease, while a predominantly fat dietary or starvation increase the susceptibility of hepatic cells to injury by chloroform. No satisfactory explanation of all of these dietary effects has been advanced. The experimental findings here presented are an effort in that direction.

The conclusions are based upon histologic and chemical evidence obtained upon albino rats, anesthetized for one hour with chloroform, and sacrificed twenty-four hours later.

The data show that the deleterious influence of high fat dietaries is related to the resulting increased hepatic lipid, which, because of the great solubility of chloroform in fat, acts as a reservoir for the chloroform; thus the concentration effective in producing injury is maintained during a longer period of desaturation.

A high concentration of hepatic glycogen, per se, fails to confer any discernible

protection against the hepatic action of chloroform. The protection afforded by carbohydrates is probably due to its activity in reducing hepatic lipid, and its protein sparing action.

The protection by protein is best explainable as due to increased body stores available to the liver for the maintenance of its integrity. The increased susceptibility of the starved animal is probably the result of depleted protein stores.

SECTION ON MEDICAL HISTORY

Regular Meeting, February 12, 1940

Report on the Meigs' Sample of Opium in the Mütter Museum.[1] Horatio C. Wood, Jr., M.D.

Edward Tyson, M.D., F. R. S., (1650–1708), Comparative Anatomist, Anthropologist, Physician, Pioneer. M. F. Ashley-Montagu*, Ph.D.

The History of Disease among the Natives of Alaska.[2] Joseph D. Aronson*, M.D.

SECTION ON OPHTHALMOLOGY[3]

Regular Meeting, January 18, 1940

Diseases of the Eye Produced by Viruses. Phillips Thygeson*, M.D.

A Case of Corneal Ulcer Associated with Lymphogranuloma Venereum. George P. Meyer, M.D., and Jacob. Reber*, M.D.

Regular Meeting, February 15, 1940

Aplasia of the Optic Nerve. Harold G. Scheie*, M.D., and A. M. Ornsteen*, M.D.

Chorio-Retinitis of the Jensen Type with Secondary Glaucoma. Thomas H. Cowan*, M.D.

Report of Two Cases of External Exudative Retinitis, Coats' Disease. Willard G. Mengel, M.D.

Histopathology of Secondary Glaucoma. Wilfred E. Fry, M.D.

The Surgical Treatment of Abducens and Trochlear Palsies. Glen G. Gibson, M.D.

SECTION ON OTOLARYNGOLOGY[4]

Regular Meeting, January 17, 1940

Symposium on Deafness. S. J. Crowe, M.D., and staff, of Johns Hopkins University

The Various Causes of High Tone Loss in Adults and Children. The General Plan of Investigation of the Study on Children. S. J. Crowe, M.D., and Curtis F. Burnam, M.D.

Anatomical Studies on the Eustachian Tube. L. M. Polvogt, M.D., and Dudley C. Babb, M.D.

Details of the Method Employed in Studying Hearing Defects in Children and the Conclusion from the First Three Months of This Study. Stacy R. Guild, Ph.D.

Relation of Hearing to Appearance of Tympanic Membrane, Nasopharynx and Operation for Removal of Tonsils and Adenoids. Jean Rose, M.D., and Harold R. Sandstead, M.D.

* *By invitation.*

[1] See Horatio C. Wood, Jr., and Arthur Osol, "Assay of a sample of opium ninety years old, with some remarks on the history of morphinometric assay", *Am. J. Pharmacy*, 1939, 111: 380–384.

[2] Printed in this (April, 1940) issue of the *Transactions & Studies.*

[3] The transactions of this Section are abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology.*

* *By invitation.*

[4] The transactions of this Section are abstracted in the *Archives of Otolaryngology.*

Regular Meeting, February 21, 1940

Symposium on Deep Infections of the Neck

ANATOMICAL CONSIDERATIONS. Oscar V. Batson, M.D.

OTOLARYNGOLOGIC FOCI. George B. Wood, M.D.

FOCI FROM TEETH AND JAW. John H. Gunter*, M.D.

X-RAY DIAGNOSIS AND THERAPY. Barton R. Young*, M.D.

GENERAL SURGICAL CONSIDERATIONS. George P. Muller, M.D.

* *By invitation.*

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

Regular Meeting, February 5, 1940

Symposium on Milk and the Public Health

MILK AND ITS RELATION TO DISEASE. A. W. Fuchs*.

THE IMPORTANCE OF CERTIFIED MILK. Julian Lyon*, M.D.

CLINICAL ASPECTS OF DAIRY-MODIFIED MILKS. Irving J. Wolman*, M.D.

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1936. DAVIS, DAVID M., 225 S. 17th St., Phila.[4]

1937. DAVIS, PERK LEE, Suite 1305, Medical Towers, 255 S. 17th St., Phila.[5]

1916. DAVIS, WARREN BEAGLE, M.D., D.SC., Clinical Professor of Oral Surgery, Jefferson Medical College; Chief of Maxillo-facial Surgery Division, Jefferson Hospital; Consulting Maxillo-Facial Surgeon, Frankford Hospital and Kensington Hospital for Women. 135 S. 18th St., Phila.

1900. DAVISSON, ALEXANDER H., 319 S. 18th St., Phila.[5]

1935. DEAVER, J. MONTGOMERY, 1830 Delancey Pl., Phila.[5]

1902. Dehoney, Howard, 240 S. 13th St., Phila.*
1935. Deibert, Irvin Elmer, 618 Benson St., Camden, N. J.
1924. Deichler, L. Waller, 1930 Chestnut St., Phila.*
1923. De Long, Perce, N.E. Cor. 20th and Chestnut Sts., Phila.*
1928. Dewees, A. Lovett, Times Medical Bldg., Ardmore, Pa.*
1924. Dillon, Edward S., 2016 DeLancey St., Phila.[6]
1932. Dintenfass, Henry, 1305 Spruce St., Phila.*
1920. Diven, John, a.b., m.d., Pediatrician in Chief, Episcopal Hospital. 326 S. 19th St., Phila.
1920. Doane, Joseph C., 19th and Spruce Sts., Phila.*
1933. Donnelly, Joseph C., 2008 Walnut St., Phila.[1]
1937. Donnelly, Robert T. M., 255 S. 17th St., Phila.[5]
1907. Dorrance, George M., 2101 Spruce St., Phila.*
1933. Downs, T. McKean, Mt. Pleasant Road, Bryn Mawr, Pa.*
1910. Drayton, William, Jr., 407 S. 22d St., Phila.[5]
1935. Duane, William, Jr., 2100 Walnut St., Phila.[5]
1935. Duncan, Garfield G., 1930 Chestnut St., Phila.[6]
1937. Dunn, Charles W., 269 S. 19th St., Phila.[4]
1935. Eads, John T., 2029 Delancey St., Phila.[5]
1911. Earnshaw, Henry C., Bryn Mawr, Pa.*
1936. Easby, Mary Hoskins, 2123 Locust St., Phila.[4]
1937. Edeiken, Joseph, 1832 Spruce St., Phila.[4]
1930. Eiman, John, Cynwyd, Pa.*
1911. Eliason, Eldridge L., a.b., m.d., sc.d., John Rhea Barton Professor of Surgery, School of Medicine, and Professor of Surgery, Graduate School of Medicine, Univ. of Pa.; Surgeon, University, Philadelphia General and Presbyterian Hospitals. 326 S. 19th St., Phila.
1939. Ellis, Van Mashburn, m.d., Assistant Ophthalmologist, Presbyterian, Wills and Orthopaedic Hospitals; Ophthalmologist, Pa. Epileptic Hospital and Colony Farm. 1530 Locust St., Phila.
1928. Ellison, Richard T., 1614 Locust St., Phila.*
1936. Ellson, J. Vernon, 255 S. 17th St., Phila.[5]
1904. Elmer, Walter G., 1801 Pine St., Phila.[5]
1937. Elsom, Kendall A., 133 S. 36th St., Phila.[5]
1934. Ely, William C., 3912 Chestnut St., Phila.[2]
1932. Engel, Gilson G., 1914 Pine St., Phila.*
1893. Eshner, Augustus A., 1019 Spruce St., Phila.*
1905. Evans, William, 500 W. Gay St., West Chester, Pa.*
1912. Eves, Curtis C., 1910 Spruce St., Phila.*
1922. Farley, David L., 1725 Pine St., Phila.*
1903. Farr, Clifford B., Bryn Mawr, Pa.[6]
1893. Farr, William W., 121 Maplewood Ave., Germantown, Phila.*
1930. Farrell, John T., Jr., 255 S. 17th St., Phila.[6]
1935. Ferguson, Lewis Kraeer, m.d., Assistant Professor of Surgery, Univ. of Pa.; Surgeon, Philadelphia General Hospital; Assistant Surgeon, Hospital of Univ. of Pa. 133 S. 36th St., Phila.
1936. Fetter, Ferdinand, 322 S. 21st St., Phila.[5]
1935. Fetter, Theodore R., 255 S. 17th St., Phila.[6]
1924. Fewell, Alexander G., 1924 Pine St., Phila.[6]
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey St., Phila.[5]

1928. Flick, John B., 1608 Spruce St., Phila.[6]

1939. Flippin, Harrison F., b.s., m.d., Instructor in Medicine, School of Medicine, Univ. of Pa.; Assistant Ward Chief, Philadelphia General Hospital. 255 S. 17th St., Phila.

1908. Fox, Herbert, m.d., Director, William Pepper Laboratory of Clinical Medicine, Univ. of Pa.; Professor of Comparative Pathology, Schools of Medicine and Veterinary Medicine, Univ. of Pa.; Pathologist to the Zoological Society of Philadelphia. Hamilton Court, 39th and Chestnut Sts., Phila.

1906. Fraley, Frederick, 71st and City Line, Overbrook, Pa.*

1939. Freeman, Norman E., b.a., m.d., J. William White Asst. Professor of Surgical Research, Harrison Dept., Surgical Research, Univ. of Pa. 320 Hathaway Lane, Wynnewood, Pa.

1935. Fridy, Cyrus Ward, 322 Riverview Ave., Drexel Hill, Pa.[4]

1933. Fritch, James Scott, 269 S. 19th St., Phila.[1]

1937. Fritz, Herbert H., Pennswood Rd. and Radnor St., Bryn Mawr, Pa.[4]

1935. Fry, Wilfred Eyles, 1819 Chestnut St., Phila.[3]

1937. Furlong, Thomas F., Jr., b.a., m.d., m.sc. (med.), Attending Otologist and Head of the Dept. of Otolaryngology, Penna. School for the Deaf, Mt. Airy, Phila.; Senior Ass't Attending Otolaryngologist and Chief of Clinic, Bryn Mawr Hospital; Instructor in Otorhinology, Graduate School of Medicine, Univ. of Pa.; Ass't Otolaryngologist to the Pennsylvania Hospital. Times Medical Building, Ardmore, Pa.

1899. Gamble, Robert G., Haverford, Pa.*

1935. Gammon, Geo. D., a.b., m.d., Associate in Neurology, Univ. of Pa 133 S. 36th St., Phila.

1931. Garner, Vaughn C., Germantown Professional Building, Phila.*

1935. Geist, Donald C., 1930 Chestnut St., Phila.[3]

1917. Gerhard, Arthur H., 1615 N. Delaware Ave., Phila.*

1899. Gibbon, John H., 1608 Spruce St., Phila.*

1934. Gibbon, John H., Jr., 1608 Spruce St., Phila.[2]

1939. Gibson, Glen Gregory, m.d., Assistant Professor of Ophthalmology, Temple University Medical School.

1933. Gifford, U. Grant, Kennett Square, Pa.*

1920. Gill, A. Bruce, 1930 Chestnut St., Phila.*

1931. Gilman, Robert Louis, 1930 Chestnut St., Phila.[6]

1927. Gilmour, William R., 6616 Woodland Ave., Phila.*

1934. Giordano, Anthony A. S., 1819 S. Broad St., Phila.*

1920. Githens, Thomas S., The Cambridge, Wissahickon and School Lane, Phila.*

1906. Gittings, John C., University Hospital, Phila.[5]

1906. Goepp, R. Max, 1201 Medical Arts Bldg., Phila.*

1933. Goldburgh, Harold L., 1932 Spruce St., Phila.[5]

1935. Goldsmith, Ralph, m.d., Attending Surgeon, Jewish Hospital. Medical Arts Bldg., Phila.

1905. Gordon, William, 1721 Pine St., Phila.[6]

1928. Gordon, Burgess L., 1832 Spruce St., Phila.*

1937. Gordon, William, 1721 Pine St., Phila.[5]

1894. Graham, Edwin E., a.b., m.d., Emeritus Professor of Pediatrics, Jefferson Medical College; Formerly Pediatrist to the Jefferson and

Philadelphia Hospitals; Past President of the American Pediatric and Philadelphia Pediatric Societies; Consulting Pediatrist to the Training School at Vineland, N. J. 1713 Spruce St., Phila.

1926. Grant, Francis Clark, 3400 Spruce St., University Hospital, Phila.[6]

1933. Greenbaum, Sigmund S., 320 S. 18th St., Phila.[6]

1932. Griffith, George C., 4028 Walnut St., Phila.[6]

1883. Griffith, J. P. Crozer, 1810 Spruce St., Phila.*

1934. Griffith, John Q., Jr., 214 Glencoe Ave., Upper Darby, Pa.[2]

1912. Griscom, J. Milton, Medical Tower, 255 S. 17th St., Phila.*

1933. Gruber, Charles M., Jefferson Medical College, Phila.[1]

1932. Guequierre, Jacques P., 1930 Chestnut St., Phila.*

1935. Hadden, Samuel B., m.d., Neurologist, Presbyterian Hospital; Visiting Neurologist, Philadelphia General Hospital; Attending Neurologist, Fitzgerald-Mercy Hospital; Associate in Neurology, School of Medicine, Univ. of Pa. 37 S. 20th St., Phila.

1935. Haines, Harlan F., 134 S. State Rd., Upper Darby, Pa.[3]

1939. Hamblock, Leonard C., a.b., m.d., Associate Gynecologist and Obstetrician, Methodist Episcopal Hospital; Associate Gynecologist, Orthopedic Hospital. 2230 S. Broad St., Phila.

1894. Hamill, S. McC., 1822 Spruce St., Phila.*

1897. Hand, Alfred, Jr., 1724 Pine St., Phila.*

1938. Hand, John G., a.b., m.d., Clinical Asst. in Surgery, Episcopal Hospital, Children's Hospital of Mary J. Drexel Home. 1724 Pine St., Phila.

1932. Harris, Stanley E., Lansdowne, Pa.*

1929. Harrison, Francis G., 1900 Spruce St., Phila.*

1933. Harrison, William John, 135 S. 17th St., Phila.[1]

1903. Hart, Charles D., 420 W. Mermaid Lane, Chestnut Hill, Phila.*

1932. Hartman, J. Calvin, 100 W. Walnut Lane, Phila.*

1926. Hartmann, Fred L., 1914 Pine St., Phila.*

1935. Haskell, Benjamin F., 1426 Spruce St., Phila.[3]

1936. Hatch, Lerleen Clement, Univ. of Pa. Hospital, 36th and Spruce Sts., Phila.[4]

1907. Hatfield, Charles James, a.m., m.d., sc.d. (Princeton '38), Associate Director, Henry Phipps Institute; Trustee, University of Pa.; President, Phila. Health Council and Tuberculosis Committee; Secretary, National Tuberculosis Association. Henry Phipps Institute, 7th and Lombard Sts.

1911. Heed, Charles R., 1205 Spruce St., Phila.*

1927. Herman, Leon, 801 Medical Arts Bldg., Phila.*

1924. Hewson, William, a.b., m.d., Assistant Professor in Otolaryngology, Graduate School of Medicine, Univ. of Pa.; Surgeon-in-Chief, Department of Otolaryngology, Abington Memorial Hospital; Otolaryngologist to the Pennsylvania Hospital; Otolaryngologist to the Children's Hospital. 6013 Greene St., Phila.

1924. Hirst, John C., 2d, 500 N. 20th St., Phila.*

1908. Hitchens, Arthur Parker, Lt. Col., M.C., U. S. A., m.d., Assistant Professor, Military Science and Tactics, School of Medicine; George S. Pepper Professor and Director of the Department of Public Health and Preventive Medicine, School of Medicine, Univ. of Pa. Dept. Public Health and Preventive Medicine, Univ. of Pa.

1939. Hodes, Philip J., B.S., M.D., Associate in Radiology, Graduate School of Medicine, Univ. of Pa.; Fellow in Radiology, Graduate School of Medicine, Univ. of Pa. X-Ray Dept., University Hospital, 36th and Spruce Sts., Phila.

1905. Hodge, Edward B., A.B., M.D., Surgeon to the Presbyterian Hospital and the Germantown Hospital; Chief Surgeon, Chester County Hospital; Associate Professor of Surgery, Graduate School of Medicine, Univ. of Pa. 2019 Spruce St., Phila.

1931. Holland, H. Albert, 8200 Crittenden St., Chestnut Hill, Phila.*

1933. Hollingshead, Irving W., 123 S. 18th St., Phila.*

1932. Hollingsworth, I. Pemberton P., 411 N. Walnut St., West Chester, Pa.*

1919. Hopkins, Arthur H., 1726 Pine St., Phila.*

1925. Hopkinson, R. Dale, Jenkintown, Pa.*

1928. Houser, Karl Musser, PH.B., M.D., SC.D., Professor Otolaryngology, Univ. of Pa. 2010 Spruce St., Phila.

1938. Howell, John Carnett, M.D., Chief Surgeon, Nazareth Hospital, Phila.; Chief Surgeon, Radiological Division, Philadelphia General Hospital; Assistant Professor of Surgery, Graduate School of Medicine, Univ. of Penna.; Assistant Surgeon, Presbyterian Hospital. 326 S. 19th St., Phila.

1908. Hoyt, Daniel M., Veterans' Bureau Hospital, St. Petersburg, Fla.*

1937. Hughes, Joseph, 4401 Market St., Phila.[5]

1939. Hughes, P. Boland, A.B., M.D., Associate in Urology, Medical School, Univ. of Pa.; Asst. in Surgery, Dept. of Urology, University Hospital; Asst. Urologist, Abington Memorial Hospital. Alden Park Manor, Germantown, Phila.

1892. Hughes, William E., 3945 Chestnut St., Phila.*

1937. Hughson, Walter, Abington Memorial Hospital, Abington, Pa.[5]

1923. Hume, John E., N.E. Corner 20th and Chestnut Sts., Phila.*

1921. Hunter, Robert John, 2011 Chestnut St., Phila.[6]

1926. Husik, David N., 1820 Spruce St., Phila.*

1934. Hustead, Frank H., 5112 N. Broad St., Phila.[5]

1898. Hutchinson, J. P., Media, Pa.*

1937. Ingle, Harry Barr, M.D., 1937 Fairmount Ave., Phila.

1935. Ingleby, Helen, Woman's Medical College, East Falls, Phila.[3]

1921. Ivy, Robert H., M.D., D.D.S., Professor of Maxillo-Facial Surgery, School of Medicine and Graduate School of Medicine, Univ. of Pa.; Chief of Maxillo-Facial Surgery, University and Graduate Hospitals; Oral Surgeon, Presbyterian Hospital; Consulting Plastic Surgeon, Children's Hospital. 1930 Chestnut St., Phila.

1917. Jackson, Chevalier, M.D., SC.D., LL.D., Honorary Professor of Broncho-Esophagology and Consultant in Broncho-Esophagologic Research, Temple University School of Medicine; President Woman's Medical College of Pennsylvania. 255 S. 17th St., Phila.

1932. Jackson, Chevalier L., A.B., M.D., M.SC. (MED.), Professor of Broncho-Esophagology, Temple University School of Medicine and Hospital; Bronchoscopist, Lankenau Hospital and Mary J. Drexel Home. 255 S. 17th St., Phila.

1934. Jacobs, Maurice S., 1831 De Lancey Place, Phila.[6]

1922. Jameson, Howard Leon, m.d., Professor of Clinical Medicine, Graduate School of Medicine, Univ. of Pa. 250 S. 17th St., Phila.
1913. Jeffreys, William H., Rosemont, Pa.*
1928. John, Rutherford L., 256 S. 21st St., Phila.*
1926. Johnson, George Ernest, 5341 Chester Ave., Phila.*
1938. Johnson, Thomas A., a.b., m.d., Instructor in Gastro-enterology, Graduate School of Medicine, Univ. of Pa. 250 S. 18th St., Phila.
1918. Jonas, Leon, 255 S. 17th St., Phila.*
1924. Jones, Harold W., 1930 Chestnut St., Phila.*
1900. Judson, Charles F., 1005 Spruce St., Phila.*
1902. Jump, Henry Draper, m.d., Attending Physician, Philadelphia General Hospital; Consulting Physician, Misericordia Hospital; Prof. Emeritus, Applied Therapeutics, Woman's Med. Coll. of Penna. 2019 Walnut St., Phila.
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.[3]
1938. Kasper, Kelvin A., 135 S. 18th St., Phila.[6]
1926. Kaufman, Isadore, 2054 Locust St., Phila.*
1923. Kay, James, 600 W. Olney Ave., Phila.*
1938. Keeler, Harold R., 1824 Spruce St., Phila.[6]
1913. Kelly, Francis J., 2211 Locust St., Phila.*
1935. Kelly, George F. J., N.E. Cor. 20th and Chestnut Sts., Phila.[3]
1932. Kelly, Herbert T., 1900 Spruce St., Phila.*
1909. Kelly, James A., 1815 Spruce St., Phila.*
1912. Kelly, Thomas C., 105 School Lane, Phila.*
1921. Kern, Richard A., a.b., m.d., Professor of Clinical Medicine, School of Medicine and Graduate School of Medicine, Univ. of Pa. University Hospital, 36th & Spruce Sts., Phila.
1935. Keyes, Baldwin L., 2025 Walnut St., Phila.[3]
1930. Kimbrough, Robert A., Jr., a.b., m.d., Assistant Professor Gynecology and Obstetrics, School of Medicine, Univ. of Pa.; Chief of Service B. Obstetrics and Gynecology, Pennsylvania Hospital; Consulting Obstetrician, Chester County Hospital. 807 Spruce St., Phila.
1936. King, Orville C., Medical Tower Bldg., 255 S. 17th St., Phila.[3]
1931. Kinney, Willard H., 315 S. 17th St., Phila.*
1920. Klauder, Joseph V., 1934 Spruce St., Phila.*
1920. Klein, Thomas, 250 S. 18th St., Phila.*
1934. Klemmer, Roland N., a.b., m.d., Chief of Medical Service, Lancaster General Hospital. 439 North Duke St., Lancaster, Pa.
1934. Kline, Oram R., 414 Cooper St., Camden, N. J.[2]
1932. Klopp, John W., 913 Medical Arts Bldg., 16th and Walnut Sts., Phila.*
1919. Knipe, Norman L., 1930 Chestnut St., Phila.*
1908. Knowles, Frank C., 2035 Spruce St., Phila.*
1938. Knox, Andrew, m.d., Chief Ophthalmic Surgeon, Episcopal Hospital; Chief Ophthalmic Surgeon, Nazareth Hospital; Consulting Ophthalmologist, State Hospital for the Insane, Norristown, Pa. 1930 Chestnut St., Phila.
1925. Knox, Harry E., 719 66th Ave., Oak Lane, Phila.*
1914. Kolmer, John A., Cynwyd, Pa.*
1936. Konzelmann, Frank Williamson, 3638 N. 21st St., Phila [3]

1932. Kornblum, Karl, 9 Hathaway Circle, Wynnewood, Pa.[6]
1904. Krauss, Frederick, 1930 Chestnut St., Phila.*
1914. Krumbhaar, Edward B., School of Medicine, University of Pennsylvania, Phila.*
1900. Krusen, Wilmer, Phila. College of Pharmacy, Phila.*
1932. Landis, Eugene M., M.D., PH.D., M.S. (Hon.), Professor of Internal Medicine, Department of Internal Medicine, University of Virginia Hospital, University, Virginia.
1907. Langdon, H. Maxwell, 1530 Locust St., Phila.*
1933 Langdon, Roy L., 5917 Greene St., Germantown, Phila.*
1934. Laplace, Louis B., Associate in Medicine, Jefferson Medical College; Physician, Misericordia Hospital; Ass't Physician, Philadelphia General Hospital; Cardiologist, Nazareth Hospital. 1900 Rittenhouse Sq., Phila.
1926. Laws, George M., B.S., M.D., Gynecologist, Presbyterian Hospital; Diplomate, American Board of Obstetrics and Gynecology. 1907 Spruce St., Phila.
1936. Leaman, William G., M.D. (F.A.C.P.)., Assistant Professor of Medicine in charge of Department of Cardiology, Woman's Medical College of Pa.; Cardiologist, Woman's College Hospital; Cardiologist, Memorial Hospital; Consulting Cardiologist, Northeastern Hospital. 3700 Baring St., Phila.
1920. Leavitt, Frederic Headley, M.D., Asst. Professor Neurology, Graduate School of Medicine and Associate in Psychiatry, Medical School, Univ. of Pa.; Chief, Dept. Psychiatry, Philadelphia General Hospital; Neuropsychiatrist, Reading Hospital, Reading, Pa. 1527 Pine St., Phila.
1934. Lee, Thomas B., 622 Cooper St., Camden, N. J.[2]
1908. Lee, Walter Estell, M.D., Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Chairman of the Editorial Board of the Annals of Surgery; Surgeon to the Pennsylvania Hospital and to the Graduate Hospital of the University of Pennsylvania. 1833 Pine St., Phila.
1936. Lehrfeld, Louis, 1321 Spruce St., Phila.[5]
1935. Lemmon, William T., 1930 Chestnut St., Phila.[3]
1920. Leopold, Simon S., 2025 Spruce St., Phila.*
1933. Levering, J. Walter, 1309 Oak Lane, Phila.[1]
1915. Lewis, Fielding O., Providence Road, Media, Pa.*
1938. Lewis, James P., 3815 Chestnut St., Phila.[6]
1936. Lillie, Walter I., 255 S. 17th St., Phila.[3]
1938. Lindauer, M. August, 5901 Warrington St., Phila.[6]
1927. Lindsey, Walter H., 810 W. Dauphin St., Phila.*
1936. Lintgen, Charles, M.D., Assistant Gynecologist, Jefferson Hospital; Assistant Gynecologist to O. P. D., Bryn Mawr Hospital. 1930 Chestnut St., Phila.
1936. Llewellyn, Thomas H., 739 N. 40th St., Phila.[4]
1907. Lodholz, Edward, Medical Laboratories, Univ. of Pa., Phila.*
1931. Loewenberg, Samuel A., M.D., Clinical Professor of Medicine, Jefferson Medical College; Assistant Physician, Jefferson Hospital; Visiting Physician, Philadelphia General Hospital, and Northern Liberties

Hospital; Consulting Physician, Philadelphia Hospital for Contagious Diseases. 1905 Spruce St., Phila.

1938. Long, Charles-Francis, 256 S. 21st St., Phila.[6]

1933. Long, Esmond R., Henry Phipps Institute, 7th and Lombard Sts., Phila.[5]

1935. Long, William L., 2025 Walnut St., Phila.[3]

1893. Longaker, Daniel Carrel, m.d., Consulting Obstetrician, Kensington Hospital for Women. Retired. 5702 Overbrook Ave., Phila.

1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.*

1936. Lucchesi, Pascal Francis, a.b., m.d., Superintendent and Medical Director, Philadelphia Hospital for Contagious Diseases; Associate in Pediatrics, Temple University Medical School; Consultant, Shriners Hospital of Philadelphia. 1838 S. Broad St., Phila.

1921. Lucké, Balduin H. E., Medical School, Univ. of Pa., Phila.*

1924. Ludy, John B., 1201 Medical Arts Bldg., Phila.*

1923. Lueders, Charles W., 1930 Chestnut St., Phila.*

1932. Lukens, Francis D. W., Cynwyd, Pa.[6]

1938. Lukens, Philip Jefferson, Jr., m.d., Associate Physician, Chestnut Hill Hospital; Consulting Internist, State Hospital, Norristown, Penna. 158 E. Butler Ave., Ambler, Pa.

1930. Lukens, Robert M., 1923 Spruce St., Phila.[2]

1929. Lull, Clifford B., Women's Bldg., Penna. Hosp., 807 Spruce St., Phila.*

1939. Luongo, Romeo A., m.s., m.d., Associate in Otolaryngology, Graduate School of Medicine, Graduate Hospital, Univ. of Pa. and Pennsylvania Hospital. 2054 Locust St., Phila.

1919. Lynch, Frank B., Jr., The Germantown Hospital, E. Wister St., Germantown, Phila.[5]

1914. Lyon, B. B. Vincent, a.b., m.d., sc.d., Associate Professor of Medicine, Jefferson Medical College; Assistant Visiting Physician, Jefferson Hospital; Chief of Clinic, Out-Patient Gastro-intestinal Dept., Jefferson Hospital. 2031 Locust St., Phila.

1933. McAndrews, Leo F., Times Medical Bldg., Ardmore, Pa.[1]

1932. McCahey, James F., 1534 Pine St., Phila.*

1900. McCarthy, Daniel J., 2025 Walnut St., Phila.*

1936. McCarthy, Patrick A., Central Medical Bldg., Phila.[3]

1935. McClenahan, William U., 3 Summit Ave., Chestnut Hill, Phila.[3]

1931. McCloskey, Edward, 7 E. Chestnut Ave., Chestnut Hill, Phila.*

1935. McConnell, James W., 20th and Chestnut Sts., Phila.[3]

1934. McCouch, Grayson P., Medical School, University of Pa., Phila.[2]

1938. McCrea, Lowrain E., 1930 Chestnut St., Phila.[6]

1937. McCutcheon, Morton, Alden Park Manor, Germantown, Phila.[6]

1895. McFarland, Joseph, 542 W. Hortter St., Germantown, Phila.*

1937. McGuinness, Aims C., The Children's Hospital, 1740 Bainbridge St., Phila.[5]

1931. McIver, Joseph, 255 S. 17th St., Phila.[3]

1933. McLaughlin, James S., 334 S. 21st St., Phila.*

1924. McMillan, Thomas M., 2044 Locust St., Phila.*

1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts., Phila.*

1932. MACFARLANE, CATHARINE, M.D., Professor of Gynecology, Woman's Medical College of Pennsylvania; Gynecologist-in-Chief, Hospital of the Woman's Medical College of Pa.; Gynecologist and Obstetrician, Philadelphia General Hospital. Medical Arts Bldg., Phila.

1910. MACKINNEY, WILLIAM H., 1930 Chestnut St., Phila.*

1936. MACMURTRIE, WM. J., 912 S. 49th St., Phila.[4]

1939. MACNEILL, NORMAN M., M.D., Asst. Professor of Pediatrics, Jefferson Medical College; Pediatrician, St. Joseph's and Jefferson Hospitals. 5116 N. 5th St., Phila.

1935. MAEDER, LEROY M. A., 206 S. 13th St., Phila.[6]

1935. MAIER, ERNEST G., 1323 N. 15th St., Phila.[5]

1914. MAIER, F. HURST, 2019 Walnut St., Phila.*

1936. MANN, BERNARD, 2019 Pine St., Phila.[4]

1937. MARGOLIES, ALEXANDER, 1836 Delancey St., Phila.[4]

1935. MASON, JAMES B., 3815 Chestnut St., Phila.[3]

1935. MATTHEWS, ROBERT A., B.S., M.D., Assistant Professor of Psychiatry, Jefferson Medical College; Psychiatrist to Institute of Pennsylvania Hospital; Visiting Psychiatrist, Philadelphia General Hospital. 111 N. 49th St., Phila.

1939. MAY, HANS, M.D., Instructor in Surgical Pathology, Graduate School of Medicine, Univ. of Pa.; Asst. Surgeon, Chestnut Hill Hospital; Clinical Associate in Surgery, Lankenau Hospital; Asst. Surgeon, Germantown Hospital. 269 S. 19th St., Phila.

1932. MEADE, RICHARD H., JR., Miquon, Pa.[2]

1934. MECRAY, PAUL M., 405 Cooper St., Camden, N. J.[2]

1914. MENCKE, J. BERNHARD, A.B., M.D., Associate Surgeon, Lankenau Hospital. 1816 Spruce St., Phila.

1923. MENDELSON, WALTER, 639 Church Lane, Germantown, Phila.*

1937. MEYER, GEORGE PHILLIP, 410 Haddon Ave., Camden, N. J.[6]

1935. MILLER, FORD A., 4016 Chestnut St., Phila.[3]

1934. MILLER, HUGH MCCAULEY, 1614 Locust St., Phila.[2]

1939. MILLER, MALCOLM W., A.B., M.D., Instructor in Medicine, Graduate School of Medicine, Univ. of Pa.; Asst. Instructor in Medicine, Allergy Dept., School of Medicine, Univ. of Pa.; Asst. Physician, Lankenau Hospital. 2021 W. Girard Ave., Phila.

1939. MILLER, MERLE M., B.S., M.D., Instructor in Medicine, Graduate School of Medicine, Univ. of Pa.; Asst. Visiting Physician, Abington Memorial Hospital; Asst. Physician in Allergy, Germantown Hospital; Attending Allergist, Bryn Mawr Hospital. 6013 Greene St., Phila.

1932. MILLER, M. VALENTINE, 114 W. Phil-Ellena St., Phila.[2]

1921. MILLER, T. GRIER, University Hospital, 36th and Spruce Sts., Phila.[5]

1937. MISSETT, JOSEPH VINCENT, JR., 1814 Spruce St., Phila.[5]

1904. MITCHELL, CHARLES FRANKLIN, M.D., Consultating Surgeon, Pennsylvania, Bryn Mawr and St. Christopher's Hospitals; Surgeon, Germantown Hospital. 2003 Pine St., Phila.

1921. MOHLER, HENRY KELLER, P.D., M.D., Dean, The Jefferson Medical College; Sutherland M. Prevost Professor of Therapeutics, Jefferson Medical College; Attending Physician to Jefferson Hospital; Physician-in-Charge of Sub-Department of Electrocardiology, Jefferson Hospital. 319 S. 16th St., Phila.

1932. Mohler, Roy W., A.B., M.D., Chief in Obstetrics and Gynecology, Methodist Hospital; Obstetrician and Gynecologist and Chief of the Out-patient Department, Philadelphia Lying-in, Pennsylvania Hospital; Associate in Gynecology, Jefferson Medical College. 1806 Spruce St., Phila.

1936. Montgomery Hugh, 216 Kent Rd., Ardmore, Pa.[4]

1936. Montgomery, John B., 1930 Chestnut St., Phila.[4]

1932. Montgomery, Thaddeus L., 1930 Chestnut St., Phila.[6]

1928. Moon, Virgil H., Jefferson Medical College, Phila.*

1935. Moore, John Royal, Beury Bldg., Broad St. and Erie Ave., Phila.[3]

1924. Moorhead, Stirling W., 1523 Pine St., Phila.[5]

1918. Morgan, Arthur Caradoc, M.D., Sc.D., Emeritus Professor of Clinical Medicine, Temple University; Active Consulting Physician to Tuberculosis Department, Philadelphia General Hospital; Consulting Physician to the Eastern State Penitentiary and to the Frankford Hospital; Former Member of the Pennsylvania State Board of Medical Education and Licensure. 501 W. Hortter St., Mt. Airy, Phila.

1936. Morgan, David R., Jefferson Medical College, Phila.[3]

1886. Morris, Caspar, Haverford, Pa.*

1893. Morris, Elliston J., 128 S. 18th St., Phila.*

1929. Mudd, Stuart, B.S., M.A., M.D., Professor of Bacteriology, School of Medicine, Univ. of Pa. Department of Bacteriology, Medical School, Univ. of Pa.

1935. Mullen, Carroll Richard, B.A., M.D., Attending Surgeon, Wills Hospital; Attending Ophthalmologist, Philadelphia General Hospital and Fitzgerald-Mercy Hospital; Instructor of Ophthalmology, Jefferson Medical College. 255 S. 17th St., Phila.

1934. Mullen, Edward A., 2615 W. Somerset St., Phila.[2]

1905. Muller, George P., 1930 Spruce St., Phila.[6]

1930. Murphy, Douglas P., 3815 Chestnut St., Phila.*

1934. Murphy, Eugene C., 1841 S. Broad St., Phila.[2]

1905. Mutschler, Louis H., 1625 Spruce St., Phila.*

1902. Nassau, Charles F., M.D., LL.D., Sc.D., Clinical Professor of Surgery, Jefferson Medical College; Surgeon, St. Joseph's Hospital; Chief Surgeon, Frankford Hospital; Consulting Surgeon, Girard College. 1710 Locust St., Phila.

1936. Nelson, Guy M., 928 Clinton St., Phila [3]

1905. Newcomet, William S., 3501 Baring St., Phila.*

1905. Newlin, Arthur, 1804 Pine St., Phila.*

1938. Newton, Zachariah B., 7109 McCallum St., Mt. Airy, Phila.[6]

1935. Nicholson, Jesse Thompson, 1614 Locust St., Phila.[5]

1899. Nicholson, William Rufus, 2023 Spruce St., Phila.[3]

1905. Norris, Charles C., 133 S. 36th St., Phila.*

1938. Norris, Robert F., Pennsylvania Hospital, 8th and Spruce Sts., Phila.[6]

1933. Nylin, Josef B., University Hospital, Phila.[1]

1913. O'Neal, Alexander Hay, St. Davids, Pa.*

1936. Orr, Theodore E., 1930 Chestnut St., Phila., Pa.[5]

1913. Outerbridge, George W., 1927 Spruce St., Phila.*

1915. Owen, Hubley R., 319 S. 16th St., Phila.*

1897. Packard, Francis R., m.d., ll.d., 304 S. 19th St., Phila.*

1933. Palmer, Harold Dean, b.s., m.d., Clinical Professor of Psychiatry, Woman's Medical College of Pennsylvania; Associate in Psychiatry, School of Medicine, Univ. of Pa.; Senior Psychiatrist, Institute of the Pennsylvania Hospital; Visiting Physician, Psychopathic Department, Philadelphia General Hospital. 111 N. 49th St., Phila.

1909. Parish, Benjamin Dores, 1927 Spruce St., Phila.[6]

1931. Paul, John Davis, a.b., m.d., Chief of Metabolic Service, Episcopal Hospital, St. Christopher's Hospital for Children, and Stetson Hospital; Pathologist, St. Christopher's Hospital for Children. 3112 N. Broad St., Phila.

1932. Payne, Franklin L., 133 S. 36th St., Phila.*

1922. Pelouze, P. S., 1737 Chestnut St., Phila.*

1909. Pemberton Ralph, Paoli, Pa.*

1930. Pendergrass, Eugene P., m.d., Director of the Department of Radiology, Univ. of Pa. Hospital; Professor of Radiology, Medical School, and Graduate School of Medicine, Univ. of Pa. 3400 Spruce St., Phila.

1932. Pennell, Howard Y., West Chester, Pa.*

1939. Pepper, D. Sergeant, m.d., Instructor in Medicine, Medical School, Univ. of Pa. 2031 Locust St., Phila.

1914. Pepper, O. H. Perry, b.s., m.d., sc.d., Professor of Medicine, School of Medicine, Univ. of Pa. University Hospital, 36th and Spruce Sts., Phila.

1902. Pepper, William, School of Medicine, Univ. of Pa., Phila.*

1916. Percival, Milton Fraser, m.d., Radiologist, Methodist Hospital; Formerly Associate Professor of Radiology, Polyclinic. 2332 S. Broad St., Phila.

1917. Peter, Luther Crouse, a.m., m.d., sc.d., ll.d., Ophthalmologist, Graduate Hospital, Univ. of Pa. and Rush Hospital for Consumption and Allied Diseases; Consulting Ophthalmologist, Friends Hospital for Nervous and Mental Diseases, and Memorial Hospital. 1930 Chestnut St., Phila.

1937. Pettit, Horace, s.b., m.d., Assistant Instructor in Medicine, Godey and Seeger Fellow in Clinical Medicine, School of Medicine, Univ. of Pa. State Road and Henry Lane, Bryn Mawr, Pa. (P. O. Box 667).

1905. Pfahler, George E., 1930 Chestnut St., Phila.*

1915. Pfeiffer, Damon B., 1822 Pine St., Phila.*

1935. Phillips, Arthur W., 3904 Walnut St., Phila.[3]

1911. Piersol, George Morris, 2031 Locust St., Phila.[6]

1933. Pillsbury, Donald M., 133 S. 36th St., Phila.[6]

1905. Pitfield, Robert L., 5211 Wayne Ave., Phila.*

1922. Pleasants, Henry, Jr., West Chester, Pa.*

1937. Polk, David Stewart, Rosemont, Pa.[5]

1932. Porter, Roland De Lance, Jenkintown, Pa.*

1931. Pryor, Charles Allen, m.d., Oto-Laryngologist, Bryn Mawr Hospital and Out-patient Clinic, Bryn Mawr Hospital; Associate Laryngologist, Pennsylvania Hospital. 1910 Spruce St., Phila.

1931. Ramsey, Frank M., Chestnut Hill, Phila.*

1913. Randall, Alexander, b.a., m.a., m.d., Professor of Urology, Univ. of

Pa.; Urologist to Abington Memorial Hospital, and Chestnut Hill Hospital. 1323 Medical Arts Bldg., Phila.

1926. RAVDIN, I. S., 3400 Spruce St., Phila.[6]

1938. READ, HILTON SHREVE, 5407 Atlantic Ave., Atlantic City, N. J.[6]

1928. REESE, WARREN S., M.D., Attending Surgeon, Wills Hospital; Assistant Professor, Graduate School of Medicine, Univ. of Pa. 1901 Walnut St., Phila.

1925. REEVES, RUFUS S., 2227 Spruce St., Phila.*

1931. REGESTER, ROBERT P., 255 S. 17th St., Phila.*

1920. REHFUSS, MARTIN E., N.E. Corner 16th and Spruce Sts., Phila.*

1921. REIFF, E. PAUL, 1927 Spruce St., Phila.[6]

1937. REIMANN, HOBART A., Jefferson Hospital, Phila.[5]

1919. REIMANN, STANLEY P., M.D., Director of The Lankenau Hospital Research Institute; Professor of Oncology, Hahnemann Medical College; Associate Professor of Surgical Pathology, Graduate School of Medicine, Univ. of Pa. The Lankenau Hospital Research Institute, Girard and Corinthian Aves., Phila.

1929. DE RÉNYI, GEORGE S., 212 S. 39th St., Phila.*

1923. REPPLIER, SIDNEY J., 373 Roumfort Rd., Mt. Airy, Phila.*

1936. RICHARDS, JAMES L., 1930 Chestnut St., Phila.[4]

1919. RICHARDSON, RUSSELL, 320 S. 16th St., Phila.*

1919. RIDPATH, ROBERT F., 1737 Chestnut St., Phila.[6]

1898. RIESMAN, DAVID, 1520 Spruce St., Phila.[6]

1936. RITTER, JOSEPH A., N.E. Cor. 54th and Gainor Rd., Phila.[4]

1933. DE RIVAS, DAMASO, Lansdowne, Pa.[1]

1932. ROBBINS, FREDERICK R., 255 S. 17th St., Phila.*

1939. ROBERTS, ELLA, B.S., M.A., M.D., Asst. Instructor in Medicine, Univ. of Pa.; Assistant in Medicine, Woman's Hospital. 133 S. 36th St., Phila.

1899. ROBERTS, WALTER, 1921 Spruce St., Phila.*

1932. ROBERTSON, HAROLD F., B.S., M.D., Assistant Visiting Physician, Philadelphia General Hospital, Methodist Hospital and St. Lukes and Children's Hospital; Instructor in Medicine, Univ. of Pa. 327 S. 17th St., Phila.

1903. ROBERTSON, WILLIAM EGBERT, 327 S. 17th St., Phila.*

1938. ROCHE, PHILIP Q., 255 S. 17th St., Phila.[6]

1912. RODMAN, JOHN STEWART, M.D., Professor of the Principles and Practice of Surgery, Woman's Medical College of Pa.; Surgeon-in-Chief, Woman's College Hospital; Surgeon, Bryn Mawr Hospital; Associate Surgeon, Presbyterian Hospital. 1726 Spruce St., Phila.

1934. ROGERS, HARRY L., Riverton, N. J.[2]

1928. ROSE EDWARD, University Hospital, 36th and Spruce Sts., Phila.*

1936. ROSE, ELIZABETH KIRK, 426 Owen Rd., Wynnewood, Pa.[5]

1909. ROSENBERGER, RANDLE C., M.D., Professor of Preventive Medicine and Bacteriology, Jefferson Medical College. Rahns, Pa.

1932. ROTHROCK, HARRY A., West Chester, Pa.*

1936. ROTHSCHILD, NORMAN, 235 S. 15th St., Phila.[3]

1933. ROWNTREE, LEONARD GEORGE, 1520 Spruce St., Phila.[1]

1937. ROXBY, JOHN B., Dept. of Anatomy, Temple University, Broad and Ontario Sts., Phila.[4]

1933. Rudolphy, Jay Besson, 230 S. 21st St., Phila.[6]
1905. Rugh, J. Torrance, 911 Medical Arts Bldg., Phila.*
1929. Ryan, William J., Medical Arts Bldg., Phila.*
1936. Sands, Joseph Evans, Rosemont, Pa.[5]
1905. Sartain, Paul J., 2006 Walnut St., Phila.*
1908. Sautter, Albert C., Germantown Professional Bldg., Phila.*
1927. Saxon, Gordon J., 5314 Spruce St., Phila.*
1906. Saylor, Edwin S., 1737 Chestnut St., Phila.*
1920. Scarlett, Hunter W., 230 S. 21st St., Phila.*
1939. Scattergood, Joseph, Jr., b.s., m.d., Clinical Staff, Chester County Hospital; Co-Partner, Marshall Square Sanitarium; Secretary, Chester County Medical Society. 115 S. High St., West Chester, Pa.
1917. Schaeffer, J. Parsons, 4634 Spruce St., Phila.*
1932. Schaffer, Howard W., 269 S. 21st St., Phila.[6]
1929. Scheffey, Lewis C., 255 S. 17th St., Phila.[6]
1929. Schenck, Harry P., b.s., m.d., Professor and Head of Department of Otolaryngology, Univ. of Pa. 1912 Spruce St., Phila.
1917. Schnabel, Truman G., 1704 Pine St., Phila.[6]
1917. Schoff, Charles H., Media, Pa.*
1928. Schofield, Frederick S., 822 Medical Arts Bldg., Phila.*
1921. Schumann, Edward A., 1814 Spruce St., Phila.*
1930. Scott, John Porter, m.d., Professor of Clinical Pediatrics, Graduate School, and Assistant Professor of Pediatrics, Medical School, Univ. of Pa.; Physician to the Children's Hospital; Pediatrist, Presbyterian Hospital. 1740 Bainbridge St., The Children's Hospital, Phila.
1917. Service, Charles A., Bala, Pa.*
1924. Shallow, Thomas A., 1611 Spruce St., Phila.[6]
1908. Shannon, Charles E. G., 1930 Chestnut St., Phila.*
1928. Sharpe, John S., Haverford, Pa.*
1928. Sharpless, Frederick C., Rosemont, Pa.*
1897. Sharpless, William T., West Chester, Pa.*
1931. Sheehan, William C., 8314 Germantown Ave., Phila.*
1932. Sheridan, Joyce T., 412 W. Durham St., Phila.*
1906. Shields, William G., 414 School Lane, Germantown, Phila.[6]
1936. Shipman, James Shelby, a.b., m.s., m.d., Attending Surgeon at the Wills Hospital; Assistant Professor of Ophthalmology, Graduate School of Medicine, Univ. of Pa.; Ophthalmologist, Cooper Hospital, Camden, N. J. 255 S. 17th St., Phila.
1935. Shoemaker, Robert, 3rd, 68 Byberry Rd., Hatboro, Pa.[3]
1896. Shoemaker, William T., m.d., Professor of Ophthalmology and Vice Dean for Ophthalmology, Graduate School of Medicine, Univ. of Pa.; Ophthalmic Surgeon, Graduate Hospital; Consultant, Pennsylvania, Germantown and Lankenau Hospitals. 2017 Locust St., Phila.
1900. Shumway, Edward Adams, b.s., m.d., Consulting Ophthalmic Surgeon, Lankenau Hospital; Honorary Consultant in Ophthalmology, Philadelphia General Hospital. 1737 Chestnut St., Phila.
1939. Shumway, Norman P., a.b., m.d., Instructor in Medicine, Univ. of Pa.; Visiting Physician, Pennsylvania Hospital and Cardiac Clinic, Bryn Mawr Hospital. Rittenhouse Plaza, Phila.
1936. Shuster, Benjamin H., 1824 Pine St., Phila.[3]

1903. Sinclair, John F., 4103 Walnut St., Phila.*
1907. Sinkler, Francis W., 1226 Medical Arts Bldg., Phila.*
1902. Siter, E. Hollingsworth, 2213 Delancey Place, Phila.*
1928. Skillern, Samuel R., 1734 Pine St., Phila.*
1933. Smelzer, Donald Campbell, Graduate Hospital, Phila.[1]
1929. Smith, Austin T., 259 S. 17th St., Phila.[6]
1933. Smith, Lauren Howe, a.b., m.d., Physician-in-Chief and Administrator, Department for Mental and Nervous Diseases, and Institute of the Pennsylvania Hospital; Associate in Psychiatry, Medical School and Graduate School of Medicine, Univ. of Pa.; Consulting Psychiatrist, Swarthmore College and Girard College. 111 N. 49th St., Phila.
1937. Smith, Lawrence Weld, Temple School of Medicine, North Broad and Ontario Sts., Phila.[6]
1936. Smith, Richard Manges, 329 S. 12th St., Phila.[3]
1927. Smyth, Calvin Mason, Medical Arts Bldg., Phila.[6]
1919. Smyth, Henry Field, m.d., dr.p.h., Professor, Industrial Hygiene, Univ. of Pa.; Consultant in Industrial Hygiene, Div. of Industrial Hygiene, Penna. Dept. of Health. 140 W. Baltimore Ave., Lansdowne, Pa.
1938. Snodgrass, L. E., 2528 N. 5th St., Phila.[6]
1935. Sokoloff, Martin J., 255 S. 17th St., Phila.[6]
1922. Solis-Cohen, Leon, 1923 Spruce St., Phila.[6]
1935. Sommer, George N. J., m.d., Medical Director, St. Francis Hospital, Trenton; Consulting Surgeon, Fitkin Memorial Hosp., Neptune, N. J. 120 W. State St., Trenton, N. J.
1933. Spackman, Edgar W., Hamilton Court, 39th and Chestnut Sts., Phila.*[2]
1928. Spaeth, Edmund B., m.d., Associate Professor, Graduate School of Medicine, Univ. of Pa.; Attending Surgeon, Wills Hospital; Ophthalmologist, Orthopedic Hospital and Infirmary for Nervous and Mental Diseases; Assistant Ophthalmologist, Rush Hospital. 1930 Chestnut St., Phila.
1937. Spangler, John Luther, Devon, Pa.[5]
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oak Lane, Phila.[3]
1897. Spiller, William G., 4409 Pine St., Phila.[5]
1929. Sponsler, Marshall B., 1934 Spruce St., Phila.[5]
1894. Stahl, B. Franklin, Haverford, Pa.*
1909. Starbuck, J. Clinton, 42 East Washington St., Media, Pa.*
1927. Starr, Isaac., b.s., m.d., Hartzell Professor of Research Therapeutics, School of Medicine, Univ. of Pa. 505 Cresheim Valley Rd., Phila.
1936. Steinfield, Edward, N.E. Cor. 18th and Chestnut Sts., Phila.[3]
1901. Stevens, Arthur A., 314 S. 16th St., Phila.*
1914. Stewart, Thomas S., Bellevue Stratford Hotel, Phila.*
1931. Stiles, Merritt H., m.d., Assistant physician, Germantown Hospital; Associate physician, Chestnut Hill Hospital. 113 W. Chestnut Ave., Chestnut Hill, Phila.
1934. Stimson, Cheney M., 167 Harvey St., Germantown, Phila.[5]
1925. Stokes, John H., 4228 Spruce St., Phila.*[6]
1928. Stokes, Joseph, Jr., 159 W. Coulter St., Phila.*

1923. Strecker, Edward A., a.b., m.a., m.d., d.sc., litt.d., Professor of Psychiatry and Chairman of the Dept. of Psychiatry, School of Medicine and Professor of Psychiatry, Graduate School of Medicine, Univ. of Pa.; Chief of Service and Consultant, Institute of the Pennsylvania Hospital. 111 N. 49th St., Phila.

1923. Stroud, William Daniel, b.s., m.d., Professor of Cardiology, Graduate School of Medicine and Associate in Medicine, School of Medicine, Univ. of Pa. 1011 Clinton St., Phila.

1937. Strumia, Max M., Bryn Mawr Hospital, Bryn Mawr, Pa.[5]

1933. Stuckert, Harry, 248 S. 21st St., Phila.*

1937. Sturgis, Margaret C., 1930 Chestnut St., Phila.[5]

1927. Sturgis, Samuel Booth, 34 W. Montgomery Ave., Ardmore, Pa.[6]

1934. Summey, Thomas J., 1930 Chestnut St., Phila.[2]

1930. Sunderman, F. William, 2210 Delancey St., Phila.*

1936. Surver, James Miller, 1832 Spruce St., Phila.[5]

1928. Swartley, William B., 6002 Greene St., Phila.*

1934. Sweeney, John A., 1900 Rittenhouse Sq., Phila.[2]

1900. Talley, James Ely, Lima, Del. Co., Pa.*

1933. Taylor, Herbert W., Haverford, Pa.[1]

1931. Taylor, Norman H., 100 W. Evergreen Ave., Phila.*

1928. Thomas, J. Earl, Drexel Hill, Pa.*

1907. Thomas, T. Turner, 1737 Chestnut St., Phila.*

1927. Thorington, J. Monroe, 2031 Chestnut St., Phila.*

1898. Thornton, Edward Q., 1331 Pine St., Phila.*

1936. Thornton, Mary Bickings-, 2703 West Somerset St., Phila.[4]

1936. Thorp, Francis Quicksall, 1367 Oxford St., Phila.[3]

1930. Thorpe, Edward S., Jr., School of Medicine, Univ. of Pa., Phila.[6]

1936. Thudium, William J., Medical Arts Bldg., Phila.[6]

1935. Tocantins, Leandro Maués, m.d., Assistant Professor of Medicine, Jefferson Medical College; Assistant Director, Division of Hematology, Jefferson College Hospital. 45 Woodale Rd., Phila.

1935. Toland, Owen J., 1806 Spruce St. Phila.[3]

1912. Torrey, Robert G., 1716 Locust St., Phila.*

1936. Towson, Charles Emory, Germantown Professional Bldg., Phila.[5]

1934. Tracy, Martha, ab., dr.p.h., m.d., Dean, Woman's Medical College of Pa.; Member of the Board of Health of Philadelphia. Woman's Medical College of Pa., Phila.

1908. Tracy, Stephen E., 1930 Chestnut St., Phila.*

1926. Tucker, Gabriel, 326 S. 19th St., Phila.[3]

1938. Tuft, Louis, m.d., Associate in Immunology, Temple University School of Medicine; Chief of Clinic of Allergy and Applied Immunology, Temple University Hospital. Formerly, Director of Penna. State Health Laboratories. 1530 Locust St., Phila.

1933. Tumen, Henry J., 2022 Spruce St., Phila.[1]

1938. Turman, Christopher M., Wyncote, Pa.[6]

1935. Turnbull, William G., Phila. General Hospital, Phila.[3]

1923. Turner, Creighton H., 1731 Pine St., Phila.*

1929. Tyson, Ralph M., m.d., Pediatrician, Pennsylvania Hospital and St. Christopher's Hospital for Children; Consulting Pediatrician, Montgomery Hospital, Norristown, Pa. and Shriners' Hospital for Crippled Children. 255 S. 17th St., Phila.

1937. Uhle, Charles A. W., 255 S. 17th St., Phila.[5]
1907. Ullom, Josephus T., Carpenter and Quincy Sts., Phila.*
1934. Ulrich, George A., 309 S. 12th St., Phila.[2]
1937. Vander Veer, Joseph B., 302 S. 19th St., Phila.[5]
1937. Van Loon, Emily Lois, 1930 Chestnut St., Phila.[4]
1933. Vastine, Jacob H. 2nd, Medical Arts Bldg., Phila.[6]
1912. Vaux, Norris Wistar, 807 Spruce St., Phila.[5]
1903. Wadsworth, William S., 3914 Baltimore Ave., Phila.*
1927. Wagers, Arthur J., 1429 Spruce St., Phila.[6]
1928. Wagoner, George W., Haverford Gables, Haverford, Pa.*
1938. Waldman, Joseph, 1930 Chestnut St., Phila.[6]
1931. Walker, Herschel C., Wynnewood, Pa.*
1906. Walker, John K., Media, Pa.[3]
1907. Walker, Warren, 1819 Chestnut St., Phila.*
1932. Walkling, Adolph A., Medical Arts Bldg., Phila.[6]
1904. Walsh, Joseph, 521 Medical Arts Bldg., Phila.*
1895. Watson, Arthur W., 2013 Locust St., Phila.[5]
1932. Watt, Charles C., Jr., 6605 Wayne Ave., Phila.*
1933. Waygood, James Jamison, 3464 W. School Lane, Phila.[1]
1903. Weber, Charles H., 250 S. 18th St., Phila.*
1930. Weeder, S. Dana., 6110 Greene St., Phila.[6]
1920. Weidman, Fred D., 20 Tenby Rd., Llanerch, Pa.[6]
1933. Weiss, Benjamin P., The Lenox, 13th and Spruce Sts., Phila.[5]
1923. Weiss, Edward, 1923 Spruce St., Phila.[4]
1935. Whelan, G. L., m.sc. (med.), Associate in Otolaryngology, Graduate School of Medicine, Univ. of Pa.; Otolaryngologist, Rush Hospital; Otolaryngologist, Eagleville Sanatorium; Bronchoscopist, Philadelphia General Hospital. 2100 Walnut St., Phila.
1921. Whitaker, William, 5448 Germantown Ave., Phila.*
1936. White, Ellen Pawling Corson-, 1820 Pine St., Phila.[4]
1925. Widmann, Bernard P., 250 S. 18th St., Phila.*
1936. Wilder, Theodore S., Germantown Professional Bldg., Greene and Coulter Sts., Phila.[4]
1936. Wilkinson, Richard Powers, 1613 S. Broad St., Phila.[6]
1914. Willard, De Forest P., 1726 Spruce St., Phila.*
1935. Willard, Dr. John Harrington, b.a., m.d., Physician-in-chief, Gastro-Enterological Service, Abington Memorial Hospital; Instructor in Gastro-Enterology, Graduate School of Medicine, Univ. of Pa.; Assistant in Medicine, Service B, Lankenau Hospital. 2022 Locust St., Phila.
1939. Willauer, George, b.s., m.d., Chief of Clinic, Division "B", Department of Surgery, Jefferson Hospital; Assistant Surgeon, Pennsylvania Hospital; Surgeon of Eagleville Sanatorium; Instructor in Operative Surgery, Jefferson Medical College. 1930 Chestnut St., Phila.
1907. Williams, Carl, School Lane and Green St., Phila.*
1924. Williams, Horace James, m.d., Professor of Otology, Jefferson Medical School; Otologist and Laryngologist, Germantown Hospital and Dispensary, Municipal Hospital, and Roxborough Hospital. 5908 Greene St., Germantown, Phila.

1937. Williams, John C., 6370 Germantown Ave., Phila.[6]
1920. Williams, Philip F., 2206 Locust St., Phila.*
1927. Williamson, Ernest G., 6353 Woodbine Ave., Phila.*
1916. Wilmer, Harry Bond, M.D., Director of Medical Services, Abington Memorial Hospital; Associate Professor in Medicine, Dept. of Allergy, Graduate School of Medicine, Univ. of Pa.; Associate Physician, Presbyterian Hospital; Director of Dept. of Allergy, Abington Memorial Hospital. 138 W. Walnut Lane, Germantown, Phila.
1921. Wilson, George, M.D., Professor of Clinical Neurology, Univ. of Pa.; Neurologist, Philadelphia General, Abington and Bryn Mawr Hospitals. 133 S. 36th St., Phila.
1937. Wilson, Ross B., 1820 S. Rittenhouse Sq., Phila.[6]
1902. Wilson, Samuel M., 1930 Chestnut St., Phila.*
1897. Wilson, W. Reynolds, Villa Nova, Pa.*
1904. Wister, James W., 5430 Germantown Ave., Phila.*
1933. Wohl, Michael G., 1727 Pine St., Phila.[1]
1918. Wolferth, Charles C., 26 Raynham Rd., Merion, Pa.[6]
1893. Wood, Alfred C., 2035 Walnut St., Phila.*
1932. Wood, Francis C., Wynnewood, Pa.*
1900. Wood, George B., N.E. Corner 20th and Chestnut Sts., Phila.*
1903. Wood, Horatio C., 319 S. 41st St., Phila.*
1897. Woodward, George, W. Willow Grove Ave., Chestnut Hill, Phila.*
1928. Wright, Carroll S., 1402 Spruce St., Phila.*
1937. Yaskin, Joseph C., 1832 Spruce St., Phila.[5]
1894. Zentmayer, William, 1930 Chestnut St., Phila.*
1895. Zimmerman, Mason W., M.D., Ph.G., Retired. 1518 Waverly St., Phila.
1933. Zulick, J. Donald, M.D., Roentgenologist to Abington Memorial Hospital and Kensington Hospital for Women; Consulting Roentgenologist to Naval Hospital. 2008 Walnut St., Phila.

Non-Resident Fellows

For degrees and titles when not listed see notation p. 392

ELECTED

1916. Bell, Rear Admiral William H., M.C., U.S.N., 5 W. Blackthorn St., Chevy Chase, Md.*
1903. Biggs, M. H., Rutherfordton, N. C.*
1936. Brown, Clark E., Santa Barbara Cottage Hospital, Santa Barbara, California.[5]
1908. Cadbury, William W., Dr. Sun Yat Sen Medical College, Lingnan University, Canton, China.*
1936. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.[3]
1937. Conaway, W. P., 1723 Pacific Ave., Atlantic City, N. J.[5]
1936. Cooper, Melbourne J., Nix Professional Building, 414 Navarro St., San Antonio, Texas.[6]

1897. Dorland, W. A. Newman, 4512 Sheridan Road, Chicago, Ill.[6]
1905. Evans, Joseph S., Jr., 1300 University Ave., Madison, Wis.*
1933. Fowler, Kenneth, 880 Fidelity Medical Bldg., Dayton, Ohio.
1935. Fretz, John Edgar, 114 N. 3rd St., Easton, Pa.[6]
1913. Gates, Nathaniel, m.d., Senior Attending Surgeon, Woman's Hospital. 10 Peterboro, Detroit, Mich.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.[6]
1902. Gwyn, Norman B., 109 Madison Ave., Toronto, Canada.*
1928. Hayman, Joseph Marchant, Jr., a.b., m.d., Professor of Clinical Medicine and Therapeutics, Western Reserve University School of Medicine; Associate Physician, Lakeside Hospital. Lakeside Hospital, 2065 Adelbert Road, Cleveland, Ohio.
1935. Hill, Emory, Professional Bldg., Richmond, Va.[6]
1892. Hinsdale, Guy, White Sulphur Springs, W. Va.[6]
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.[4]
1936. Hughes, Brady A., 5005 42d Place, North; Birmingham, Ala.[4]
1912. Hunter, John W., McDaniel, Md.*
1885. Jackson, Edward, a.m., sc.d., Professor Emeritus, Ophthalmology, Univ. of Colorado. Republic Building, Denver, Colorado.
1900. Jopson, John H., Waverly Mills, S. C.*
1887. Kelly, Howard A., 1418 Eutaw Place, Baltimore, Md.*
1935. McGuire, Hunter H., 105 N. Braddock St., Winchester, Va.[3]
1900. McReynolds, Robert Phillips, 213 S. Broadway, Los Angeles, Cal.*
1911. Meigs, Edward B., 1736 M St., N.W., Washington, D. C.*
1936. Middleton, William Shainline, m.d., Professor of Medicine and Dean, University of Wisconsin Medical School; Physician, State of Wisconsin General Hospital. State of Wisconsin General Hospital, Madison, Wis.
1917. Mitchell, A. Graeme, Childrens' Hospital Research Foundation, Cincinnati, Ohio.[6]
1915. Musser, John H., 1430 Tulane Ave., New Orleans, La.[3]
1937. Nicholson, Samuel T., 2d, The Hill School, Pottstown, Pa.[4]
1905. Norris, George W., Dimock, Pa.*
1901. Norris, Henry, Waverly Mills, S. C.*
1899. Parke, Wm. E., a.b., m.d., Retired. 5637 LaGorce Drive, Miami Beach, Florida.
1926. Paul, John Rodman, Dept. Internal Medicine, Yale University, New Haven, Conn.*
1907. Price, George E., Stimson Bldg., Seattle, Wash.*
1904. Ravenel, M. P., 203 Westmont Ave., Columbia, Mo.*
1936. Reisinger, John A., 6355 31st St. N.W., Washington, D. C.[6]
1907. Royer, B. Franklin, The Hall, R. D. 7, Chambersburg, Pa.*
1913. de Schweinitz, George L., 85 E. Broad St., Bethlehem, Pa.*
1908. Shoemaker, Harlan, a.b., m.d., Senior Surgeon, Los Angeles General Hospital; Clinical Professor of Surgery, University of Southern California; Trustee, Los Angeles County Medical Association. 1930 Wilshire Blvd., Los Angeles, California.
1932. Siegel, Alvin Erdreich, a.b., m.d., Attending Physician, Macon Hospital; House Physician, Hotel Dempsey; Designated Examiner, Veterans Administration. Medical Arts Building, Macon, Ga.

1933. Southworth, Varnum C., 138 Race St., Cambridge, Md.
1934. Stewart, Sloan G., Pacific and N. Carolina Aves., Atlantic City, N. J.[5]
1900. Swan, John M., 457 Park Ave., Rochester, N. Y.*
1913. Vail, William Penn, Blairstown, N. J.*
1897. Veasey, Clarence Archibald, a.m., m.d., Ophthalmic Surgeon to the Deaconess and St. Luke's Hospitals, Spokane. 1569 Paulsen Medical and Dental Bldg., Spokane, Washington.

Honorary Fellows

Limited to Fifty, of Whom Twenty May Be Foreigners

American

ELECTED

1909. Crile, George W., m.d., Cleveland Clinic, Euclid Ave. at E. Ninety-third St., Cleveland, O.
1916. Estes, Wm. L., a.m., m.d., sc.d., Surgeon Emeritus, St. Lukes Hospital. Union Bank Building, Bethlehem, Pa.
1917. Miner, Charles Howard, b.s., m.d., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanitarium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1936. Richards, Alfred Newton, ph.d., sc.d., m.d. (hon.), l.l.d., Professor of Pharmacology, School of Medicine, Vice-president in charge of Medical Affairs, Univ. of Pa. School of Medicine, Univ. of Pa., Phila.
1937. Zinsser, Hans, a.m., m.d., d.sc., Professor of Bacteriology and Immunology, Harvard Medical School. Harvard Medical School, Boston, Mass.

Foreign

1928. Archibald, Edward, m.d., McGill University, Montreal, Canada.
1937. Dale, Sir Henry Hallett, c.b.e., f.r.s., m.a., m.d., f.r.c.p., Director, National Institute for Medical Research, Hamstead, Eng. Mt. Vernon House, N.W.3, Hamstead, London.
1924. Hopkins, Sir F. Gowland, m.d., Biochemical Department, University of Cambridge, Cambridge, England.
1922. McCarrison, Sir Robert, kt., c.i.e., m.d., d.sc., ll.d., f.r.c.p., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.
1928. Rolleston, Sir Humphrey, bart., g.c.v.o., k.c.b., m.d., d.c.l. (*Durh.*), ll.d., d.sc., Martins, Haslemere, Surrey, England.

Necrological List, 1939

Herman B. Allyn. November 6, 1939.
David R. Bowen. September 6, 1939.
George M. Boyd. May 20, 1939.
Albert C. Buckley. August 17, 1939.
Charles N. Davis. October 21, 1939.
John McCrea Dickson.* September 16, 1939.
Robert N. Downs, Jr. February 9, 1939.
Louis D. Englerth. August 16, 1939.
Henry M. Fisher. April 27, 1939.
Collin Foulkrod. November 16, 1939.
Ellis E. W. Given. May 11, 1939.
Edward H. Goodman.* March 6, 1939.
Charles P. Grayson. August 16, 1939.
Walter D. McCaw.** July 7, 1939.
William J. Mayo.** July 29, 1939.
D. J. Milton Miller. July 6, 1939.
Thomas R. Neilson. October 25, 1939.
Henry K. Pancoast. May 20, 1939.
Alfred Stengel. April 10, 1939.

James J. Quiney.* March 31, 1937.

Elections to Fellowship, 1939

H. D. Barnshaw.[3]
Harvey Bartle, Jr.[2]
Frieda Baumann.[2]
Raymond W. Brust.[3]
George W. Chamberlin.[4]
Robert Kyun Hyun Charr.[2]
Emmet Frederick Ciccone.[4]
Bernard I. Comroe.[1]
Van Mashburn Ellis.[4]
Harrison F. Flippin.[2]
Norman E. Freeman.[1]
Glen Gregory Gibson.[3]
Leonard C. Hamblock.[1]
Philip J. Hodes.[4]
Patrick Boland Hughes.[3]
Romeo A. Luongo.[1]
Norman Merle Macneill.[3]
Hans May.[2]
Merle Middour Miller.[1]
Malcolm W. Miller.[4]
D. Sergeant Pepper.[3]
Ella Roberts.[4]
Joseph Scattergood, Jr.[1]
Norman Price Shumway.[3]
George Willauer.[3]

* Non-resident Fellow.
** Honorary Fellow.

[1] January 9, 1939.
[2] March 1, 1939.
[3] May 3, 1939.
[4] October 4, 1939.

TRANSACTIONS & STUDIES

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Faulty Disposal of Streptococcus Hemolyticus in Relation to the Development of the Rheumatic Lesion*†

By Alvin F. Coburn, M.D.

INTRODUCTION

THE honor which you bestow on me by inviting me to deliver this lecture carries with it the opportunity to present some of the problems of rheumatic fever. To use this opportunity constructively, I have chosen to outline a working hypothesis rather than confine myself merely to a report of facts. I have two objectives—first, to explain our concept of the nature of the disease; and, second, to indicate possible points of attack, which I hope may be fitted into your own excellent facilities for the investigation of disease.

I shall begin by reviewing briefly the close epidemiological relationship that exists between rheumatic fever and streptococcus infections of the upper respiratory tract. Both in Europe and America, the incidence of streptococcus respiratory infections is sharply seasonal, as shown by Figure 1. The peak in Europe occurs about 4 months earlier than it does here. Similarly, the peak of rheumatic fever in each continent follows closely that of scarlet fever, occurring four months earlier in Europe than in America. Epidemics of tonsillitis both in Europe and in America are known to be followed by outbreaks of rheumatic fever (Figure 2). Furthermore, when initial attacks of rheumatic fever occur in individuals recently migrated to New York City from the tropics, these attacks are preceded by acute pharyngitis. Recrudescences of rheumatic fever have, in our experience, followed hemolytic streptococcus infection of the upper respiratory tract. All of the evidence points to the importance of hemolytic streptococcus in the development of rheumatic fever.

There is, nevertheless, a striking disproportion between the incidence of

* Mary Scott Newbold Lecture XLVII, The College of Physicians of Philadelphia, March 6, 1940.

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hemolytic streptococcus infection and the incidence of rheumatic fever. Probably all inhabitants of this environment contract streptococcal infections. However, only a small percentage, certainly less than five, manifests acute rheumatism. It therefore seems that there must be factors other than infection on which the development of rheumatic fever is based and without which hemolytic streptococcus cannot produce the syndrome.

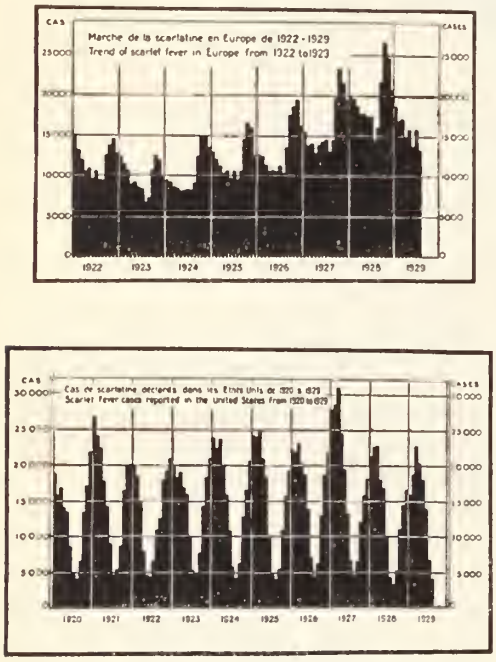


Fig. 1. The Seasonal Incidence of Scarlet Fever in Europe and in the United States—Reported by the League of Nations.

The high familial incidence and hereditary tendency to rheumatic fever is well recognized. The recent studies by Wilson and Schweitzer (1) have shown that susceptibility to rheumatic fever is transmitted as a Mendelian recessive character. Our own observations are in accord with this concept; however, we do not know at what point the hereditary factor operates. So far as we can determine, it does not affect susceptibility to streptococcal infection and we are of the opinion that its effect may well be on the host's response to this infection. A second factor is environmental. This lies concealed in a complex of conditions which militate against complete recovery from upper respiratory disease; such as inadequate diet, overcrowding, little sunlight, inhalation of traumatizing particles, and improper care of minor respiratory infections.

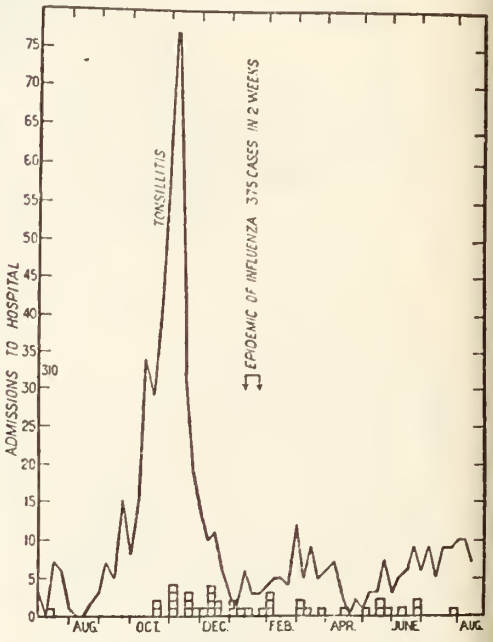


Fig. 2. The Relation of an Outbreak of Rheumatic Fever to an Epidemic of Tonsillitis—Reported by Glover, Lancet, March 8, 1930.

Susceptibility to rheumatic fever depends on a combination of these two factors. This automatically confines the disease to a limited fraction of the population. It explains the disproportion in incidence between acute rheumatism and streptococcal respiratory infections; but it throws no light on the mechanism whereby such a combination of constitu-

tional and environmental factors conditions the individual to the development of rheumatic fever. We have attempted to elucidate this mechanism and have developed the concept that rheumatic fever is an expression of faulty immunity. Certain observations which have led to this hypothesis will now be presented.

I. DEPARTURES FROM NORMAL IN THE RHEUMATIC RESPONSE, AS JUDGED BY CIRCULATING ANTIBODY

One of the most perplexing aspects of the streptococcus-rheumatism relationship has been the fact that in known rheumatic subjects, suppurative lesions or highly invasive infections do not give rise to acute rheumatism. Its development classically follows a mild upper respiratory infection, from which the patient has made a satisfactory clinical recovery. It seems possible to us that this kind of infection is handled differently by the host, and that his immune response to the mild pharyngeal sensitizing type of infection might be the critical factor. To investigate this possibility, we have therefore examined the antibody responses both of normal and rheumatic individuals following streptococcal infections of the upper respiratory tract.

The most satisfactory antibodies for this study have been those that could be measured quantitatively; hence this discussion will be confined mainly to the group-specific antistreptolysin. Since the findings of various authors have shown that several of the rheumatic immune responses are abnormal, let us see in what these abnormalities consist.

1. Antistreptolysin formation: It has been shown by a number of observers that streptococcus infection in most individuals causes a rise in the titer of circulating antistreptolysin. In the absence of suppurative complications, the titer of this antibody usually reaches its maximum within three weeks of the onset of infection. In contrast, most patients with rheumatic fever show progressive increases in titer for many weeks after recovery from infection. This point will be discussed later in detail.

2. Antifibrinolysin: Patients with rheumatic fever show an elevated antifibrinolysin level for months after infection. According to Boisvert (2) this is different from patients with uncomplicated scarlet fever.

3. Anti-M precipitin formation: Swift and Hodge (3) found a delayed increase in this type-specific antibody in rheumatic patients as contrasted with non-rheumatic subjects following uncomplicated streptococcus respiratory infections; and our observations are in accord.

4. Antistreptolysin-S formation: Recent observations of Todd and his collaborators (4) show that children with severe rheumatic activity have relatively low antistreptolysin-S titers. This is the only evidence of an antibody deficiency in rheumatic fever.

5. Serum complement: Finally, we have observed a diminution in serum complement just before the onset of the rheumatic attack. This is not seen following uncomplicated streptococcal pharyngitis and suggests the occurrence of an antigen-antibody reaction.

In summary, antibody development in the rheumatic patient seems delayed and prolonged as compared with that of non-rheumatic subjects following hemolytic streptococcus infections. The patient with severe rheumatism is deficient in neutralizing antibody to the powerful hemotoxin of streptococcus. The composite picture points to the occurrence of antigen-antibody reactions weeks after recovery from a mild pharyngeal infec-

tion. We shall now attempt to describe one of these abnormalities in detail.

The Antistreptolysin Curve and the Development of a Rheumatic Attack. We have already stated that only a small percentage of individuals who contract streptococcus infections is susceptible to the development of rheumatism. Now we wish to determine why the rheumatic subject does not develop an attack every time that he contracts pharyngitis. To this end we have attempted to establish a differential between rheumatic subjects who escape and those who develop attacks following Group A hemolytic streptococcus pharyngitis; and one difference between their antibody responses to infection has come to light. That is the following: Patients who contract hemolytic streptococcus pharyngitis and subsequently escape attacks usually show no increase in circulating antistreptolysin later than two weeks after infection; whereas patients who develop attacks usually show an increase in antistreptolysin during the third week, which progresses as long as the disease process is active. This point was emphasized in 1935 (5, 6), and during the next three years we had the opportunity to study about fifty subjects with repeated throat infections and amplify the data. So far as could be determined, the serological types of the organisms were the same in the infections followed by attacks and those followed by good health. The antibody responses, however, were different. Patients with attacks usually showed one of three types of curves. The striking difference was that rheumatism accompanied a rising titer; while it failed to develop when the titer remained stationary or fell. It is seen in Figure 3 that there were 96 infections with 62 rheumatic attacks. The onset of typical polycyclic attacks was accompanied in 41 instances by rising titers and in 9 instances by no change in titers until a second or third cycle developed. The onset of the 7 monocyclic attacks was accompanied by a rapidly rising titer, reaching its peak within two weeks after symptoms appeared; within four weeks after pharyngitis. Fifty-seven of these 62 patients showed an increase in circulating antibody during the rheumatic attack. In contrast, 31 of 34 patients who escaped attacks showed no increase in circulating antibody later than two weeks after pharyngitis. In 18 the infection was followed by a stationary or falling titer; in 10, by a rapid rise to its peak where it remained for weeks; in 3, by a rapid rise and sharp fall. These three types of titer curves are characteristic of non-rheumatic subjects recovering from hemolytic streptococcus pharyngitis. Since the same individuals developed and escaped rheumatism and since the infecting organisms in both groups were of the same serological types, we feel that the difference in antibody response is significant.

This difference is again illustrated by our 1939 group of 129 known rheumatic subjects. Forty-three contracted hemolytic streptococcus infections; half developed attacks, and half escaped. Nearly all of those who escaped completed their rise in titer within two weeks after infection; whereas those who developed attacks showed progressive titer rises, with one exception, for many weeks after the acute infection. The percentage of patients with rising titers and the average increase in titer in relation to time after pharyngitis are shown in the following table.

The simplest explanation for this continuous development of antibody for weeks after pharyngitis has subsided would be the persistence of subclinical

infection with the pharyngeal strain. If this is so, it should be possible, at least under favorable conditions, to obtain direct evidence of the agent in the host's tissues, even though the strain may have disappeared from the mucous membrane, shortly after recovery from pharyngitis. The opportunity to determine this point rarely presents itself; however, when bacteriological examination of infected tis-

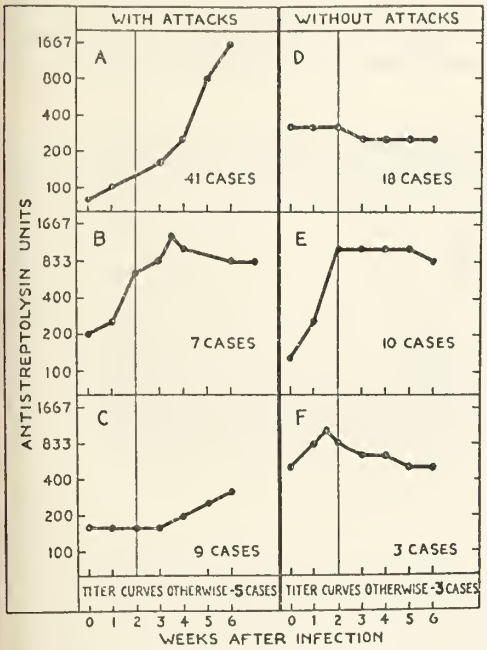


FIG. 3. THE ANTISTREPTOLYSIN RESPONSES IN RHEUMATIC SUBJECTS FOLLOWING STREPTOCOCCAL PHARYNGITIS (FINE LINE INDICATES TIME OF EXPECTED ATTACK).

sues has been feasible during life, we have recovered the infecting strain in pure culture. The post-mortem findings of Green (7) and Collis (8) have supported the concept that the infecting organism persists, not only in the deep pharyngeal tissues but also in sites remote from the upper respiratory tract. The observations of Green, if confirmed, are especially interesting since he cultured from rheumatic verrucae organisms which were of the same serological type as the strain isolated from the pharynx during life. These organisms were living in the tissues without giving rise to suppuration.

The Antistreptolysin Curve and Recovery from a Rheumatic Attack. Having pointed out that the development of rheumatic fever is accompanied by an abnormal continuation of antibody formation, I should now like to show that recovery

TABLE 1

Increase of antistreptolysin titer in relation to time after infection in patients who escaped and developed rheumatic attacks

Weeks after onset of pharyngitis	1	2	3	Later
Per cent of patients with rise of antistreptolysin titer				
Escaped	40	20	25	5
Developed rh. attack	30	50	80	90
Average increase in titer (expressed as no. of tubes* per patient)				
Escaped	1.1	.2	.3	.1
Developed rh. attack	.9	1.3	1.7	3.4

* In these titrations a rise of one tube corresponds to an increase of 0.1 in the $\log_{10}$ of the titer (6).

from a rheumatic attack is accompanied by a cessation in antibody formation. The following cases illustrate this point.

These two patients, L. G., and L. G., were American-born girls of Italian parents. Both had the same surname and christian name. Both contracted hemolytic streptococcus† pharyngitis on March 13. Both developed a rheumatic attack on April 3. The physical examination on hospital admission showed that both had tremendously enlarged hearts, both with aortic stenosis and

† Different serological types.

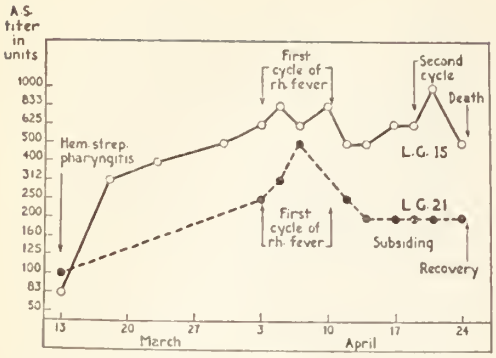
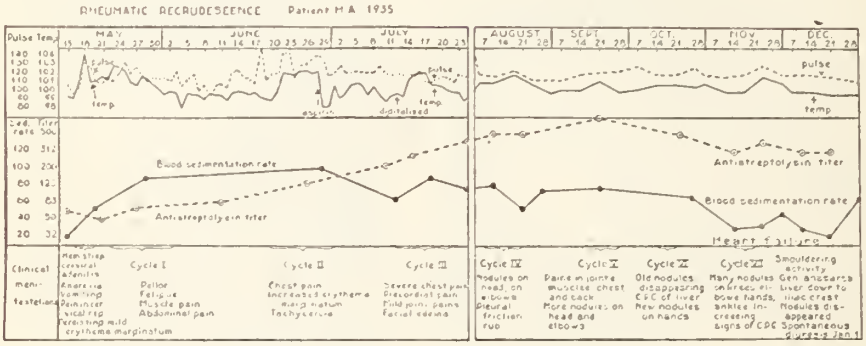


Fig. 4. The Antistreptolysin Curves in Two Patients with Different Clinical Courses

Figure 4 shows that their titer curves and courses were similar until April 14. At this time the titer of L. G., 15, rose again. This was accompanied by a fatal cycle of rheumatic fever. In contrast, there was no further rise in L. G., 21, and she made a rapid recovery.

The next two patients, E. G. and H. A., were seven year old girls, clinically similar, who had adjoining beds in a convalescent home. They both contracted pharyngitis on the afternoon of May 15, 1935, with the same agent appearing in their throat flora. Their titer curves and clinical courses were parallel for many months.



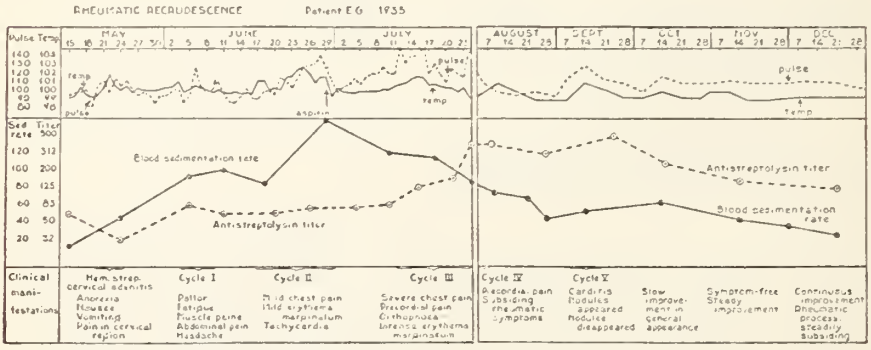


Fig. 5. The Antistreptolysin Curves in Two Patients with Similar Clinical Courses

insufficiency, mitral stenosis and insufficiency. Both had a typical cycle of rheumatic activity. At the end of this, April 14, their courses diverged. L. G., age 21, recovered rapidly. L. G., age 15, had a second cycle in which carditis was fatal.

It is seen in Figure 5 that recovery was delayed and that antistreptolysin production continued until recovery began.

Another case history illustrates the

common phenomenon of a sharp fall in the antistreptolysin titer on recovery from a rheumatic attack.

This 15 year old girl, J. H., had been under our observation for three years. The rheumatic process was quiescent when in January 1935 she contracted hemolytic streptococcus pharyngitis. This was followed two weeks later by a fulminating rheumatic attack from which she recovered satisfactorily. Another throat infection in October failed to induce an attack. However, pharyngitis in January 1936 with still another strain was followed by a rheumatic attack which began insidiously, persisted for months, and concluded with the development of a cycle with hyperpyrexia.

It is seen in Figure 6 that even though these two attacks were quite different in character and duration, improvement in each was accompanied by a falling titer and recovery by a sharp drop in the antistreptolysin level. Each of these cases illustrates that when rheumatic fever is active, the patient is producing antibody to streptococcus and that when the disease becomes inactive, antistreptolysin production stops.

The foregoing observations suggest that rheumatic activity depends both on upper respiratory infection with hemolytic streptococcus and on continued antibody production by the host. The latter seems to be an essential aspect of the immunological picture, and is independent of the character of the antistreptolysin response during the first two weeks after infection. We interpret this phenomenon as indicating continued antigenic activity of the organism. However, before attempting to go into our hypothesis as it relates to the continued production of antibody, I should like to digress to call your attention to the mechanism of a disease syndrome which has been studied experimentally.

If the development of rheumatic fever is associated with an abnormal immune response of the host, we might expect to find comparable disease syndromes following other acute infections. Such a syndrome should not appear where there is an overwhelming, virulent infection, nor in the highly immune host. It should be found among the intermediates. In our opinion, comparable phenomena do occur in tuberculosis and syphilis. There is still another disease, however, which seems to me especially pertinent to our problem, and may serve as a useful, if loose, analogy. It is post-diphtheritic paralysis. As you know, human subjects

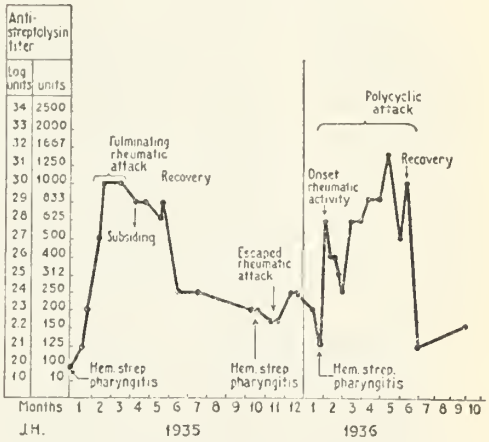


Fig. 6. The Antistreptolysin Curve in a Patient with Two Attacks, Differing in Duration.

occasionally develop paralysis about two weeks after recovery from mild diphtheria, and the phenomenon can be reproduced regularly in guinea pigs by the introduction of partially neutralized diphtheria toxin. The studies of Prigge (9) (10) have thrown light on the mechanism of this syndrome. Toxin alone, antitoxin alone, or completely neutralized toxin, will not produce paralysis. However, Prigge was able to produce the syndrome by repeated small doses of toxin. He suggests that the previously observed effectiveness of incompletely neutralized

toxin is due to a splitting of the toxin-antitoxin mixture, with intermittent liberation of small amounts of free toxin. This seems reasonable, since it is well known that human subjects dissociate toxin-antitoxin mixtures. I present this analogy to illustrate a post-infectious disease syndrome which is produced by sterile material, which takes two weeks to develop, and which is dependent on an incomplete neutralization of bacterial products.

The student of rheumatic fever is handicapped by the lack of an experimental animal. However, he does have ample opportunity to examine the histological changes which result from this disease process. An understanding of these changes may help us to understand the character of the disease. I shall therefore review our concept of these lesions so that we may finally link together agent, host response and morbid anatomy.

II. THE HISTOLOGICAL PICTURE OF RHEUMATIC ACTIVITY

The problem with which we are now confronted is how the development of streptococcus antibodies in the rheumatic subject is related to the formation of lesions. The simplest explanation would be recurrent chronic* infection comparable to recurrent erysipelas. If rheumatic lesions were chronic focal infections, activated periodically, we would expect to find in them histological evidence of the infectious agent. To this end let us examine the rheumatic lesion.

The Aschoff body has been accepted as diagnostic of rheumatic fever. The lesions are limited to areas in the vicinity of small arteries. As described by many observers, rheumatic tissues prepared by ordinary histological techniques involving acid fixation and ordinary stains show swelling of the collagen bundle, loss of fibrillar structure, and assumption of staining properties suggestive of fibrin. Klinge has called the process "fibrinoid swelling." He has shown, however, that if the tissue is impregnated with silver, the fibrillar structure can still be demonstrated, and concludes that fibrinoid swelling affects not collagen fibrils proper, but a "ground substance" in which they are presumably imbedded. Some observations of E. M. Kapp in this laboratory are entirely in accord with Klinge's interpretation. In unfixed frozen sections of typical rheumatic lesions stained with toluidine blue, the fibrillar nature of swollen collagen bundles is perfectly evident. The staining reaction is that of mucoids in general with dyes of the thionine series (11). We have observed, however, that in patients who die within ten days, before the processes of repair have become evident, definitive Aschoff bodies are absent. In such patients the myocardial lesions have the distribution typical of Aschoff bodies but consist only of areas of swollen collagen. Even in these young lesions the staining properties of the collagen bundles are already modified so as to resemble fibrin. It seems to us that the apparent damage to collagen fibrils really consists in an alteration of the mucoprotein ground substance. The exact nature of the change is a problem in protein chemistry. It has not been possible to demonstrate bacteria in any stage of Aschoff body formation.

The changes just described are illustrated by the cross section of a papillary muscle of a girl dying one month after the onset of an intense rheumatic attack. The low power photomicrograph, Figure 7, shows the disappearance of the

* Our bacteriological studies show that each recrudescence follows a new infection; that is, an organism of different serological type.

normal structure due to marked swelling and cellular infiltration. Under higher magnification, Figure 8, fragmentation of collagen fibrils and infiltration of Aschoff cells are to be seen. This establishes the diagnosis of rheumatic fever. It is again observed that there is marked edema and infiltration with mononuclear cells. The endothelium, however, is intact. The inflammatory reaction begins and is most intense at the site of the *sub*endothelial cells, involving collagen fibrils and muscle cells in close proximity, but not those in the center of the papillary muscle.

Acute valvular lesions show similar changes in the subendothelial structures. Plaques of material staining like fibrin appear to arise underneath the endothelial layer causing it to protrude into the blood stream. These changes in ground substance and endocardium represent the fundamental lesions of rheumatic activity. They take place in close proximity to circulating blood.

Histological searches for bacteria in all of these tissues have been consistently unsuccessful; yet the lesions show intense inflammation. If these lesions do not result directly from bacterial damage, what is their cause? They develop in close proximity to highly phagocytic cells of the reticulo-endothelial system such as the subendothelial histiocytes. They develop at a time when the reticulo-endo-

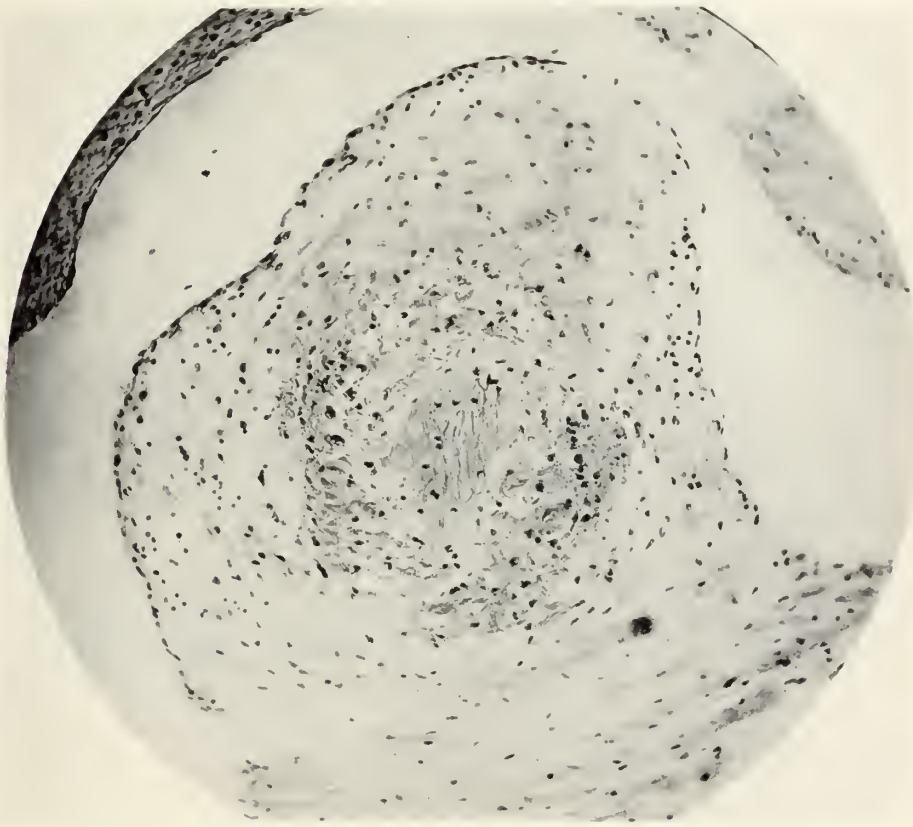


Fig. 7. Low Power Photomicrograph of Columna carnae in Rheumatic Fever

thelial system is releasing abnormally large quantities of serum proteins, especially fibrinogen (12) and gamma globulin (13). In brief, the appearance of the lesions coincides both in distribution and in time with abnormal activity of reticulo-endothelial cells.

It is interesting that Aschoff, who contributed so much to the rheumatic problem, was one of the first to emphasize the important phagocytic power of endothelial and mononuclear cells (14). Sabin (15) feels that phagocytic power is associated with the capacity of these cells to develop deciduous "surface films." Her observations have shown that the degree and location of phagocytic activity

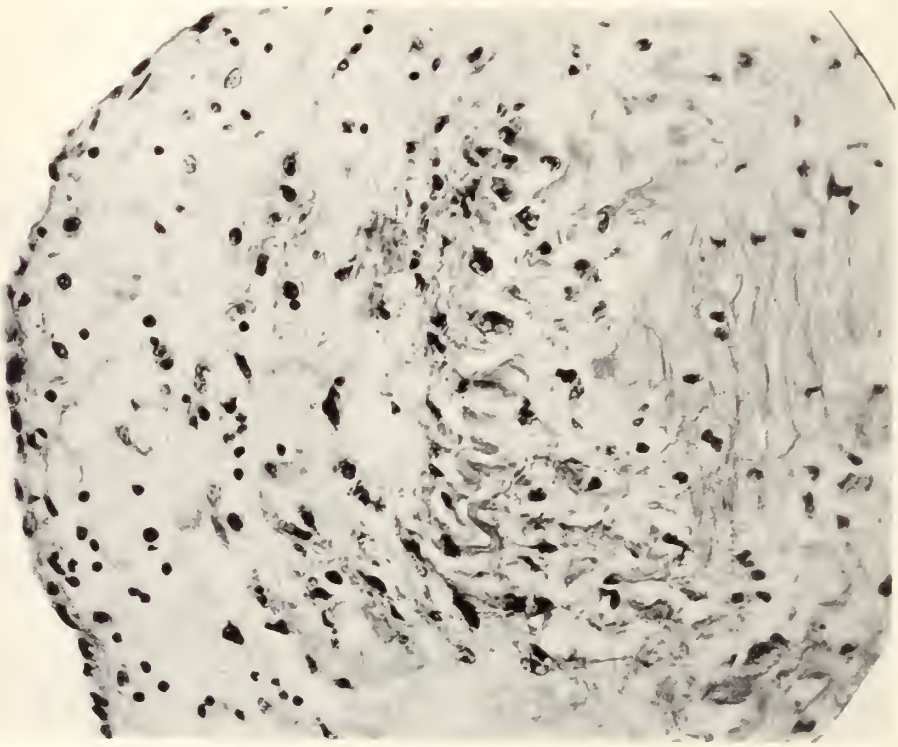


Fig. 8. Higher Magnification of the Lesion Showing (a) Intact Endothelium (b) Oedematous Subendothelium (c) Aschoff Cells Near Fragments of Collagen (d) Myocardial Fibers

III. THE RETICULO-ENDOTHELIAL SYSTEM AND ITS POSSIBLE SIGNIFICANCE IN RHEUMATISM

Function of R.E. Cells. The question which now arises in our minds is, what bearing can the state of the reticulo-endothelial system have on the development of rheumatic lesions. In a preliminary discussion of this question, I should like to consolidate certain observations and concepts of other workers.

depend on the route of absorption of the foreign material. If it is injected intravenously, phagocytosis takes place in the liver's Kupffer cells, splenic sinus cells, or bone marrow. If it enters through the lymphatics, phagocytosis occurs in the lymphatic sinus cells. If it is absorbed via connective tissues, phagocytosis is effected by histiocytes; and if via the skin, by macrophages. Sabin is of the impression that in young or in embryonic tissues the endothelial cells are the important phagocytes; in adult life the Kupffer cells become especially important. Haurowitz and Kraus (16) have found that protein "chemically labeled" with arsenic is fixed in the liver of rabbit and guinea pig. Sieg-

mund (17) and Pfuhl (18) and others have demonstrated the phagocytosis of foreign substances by subendothelial histiocytes, and De Vecchi (19) was able to damage histiocytes and cause subendothelial inflammation with mononuclear cell infiltration by injecting Trypan blue followed by bacteria or toxins.

The Handling of Antigen by Reticulo-endothelial Cells. Sabin's concept, which is a result of her histological observations on a red dye-protein, may be described briefly as follows: Antigenic matter is engulfed by a reticulo-endothelial cell. The antigen is a foreign substance, and cannot be used by the cell without modification. After digestion in the vacuoles of the phagocyte, it passes in soluble form into the cell's cytoplasm. There, in some way, it increases globulin synthesis. The cell then sheds a part of the newly formed globulin from its surface film. That part of the globulin which has the capacity to react with the antigen is antibody. If the cell discharges all of this newly synthesized antibody globulin, the host enjoys immunity. If, however, the cell retains some of the antibody globulin in its cytoplasm, it may then be expected to react differently from the normal cell when confronted with the phagocytosis of more of the same antigen. Such a cell is "sensitized."

An Explanation of Sensitization. In the light of the above mechanism, sensitization may be considered as constipation of the reticulo-endothelial cell. A sensitized cell has been able to engulf and absorb antigen, and to synthesize globulin. It has failed, however, to evacuate this globulin completely and so retains reactive material within its cytoplasm. If this cell again phagocytoses the specific antigen an abnormal intracellular reaction occurs which might be considered as cellular indigestion. This disturbance then gives rise to inflammation.

According to this hypothesis the retention of antibody globulin by the cells is not sufficient to damage the cells. For an intracellular reaction to occur, it is essential that such a cell engulf more antigen*. If sensitization, as here conceived, is a part of the rheumatic mechanism we must show that new antigen is being released at a time when the R-E cells still contain antibody. The direct demonstration of antigen in the circulation is almost impossible in infectious diseases. However, it must be assumed to be present if specific antibody is produced. We have evidence that two types of antigens circulate in certain phases of rheumatic fever, each of which might evoke an abnormal reaction. The observations are as follows:

We have already outlined our reasons for believing that streptococcus products are released during active rheumatism and it may well be that such substances are responsible for sensitization. There is also a good possibility that a secondary antigen derived in some way from the patient's tissues may be involved.

The occurrence of antigens derived from host tissues has been demonstrated by a number of workers. Burky (20) made lens substance antigenic by combining it with staphylococcus toxin. Schwentker and Rivers (21) have shown that homologous brain may become antigenic. Hughes (22) detected evidence of a secondary antigen in patients with yellow fever. Landsteiner (23) in his studies on sensitization of animals with simple chemical compounds has shown a connection between sensitizing capacity and lability of certain chemical groupings, indicating the formation of conju-

* The parenteral injection of foreign proteins may induce an intracellular reaction at this point. We have observed patients with active rheumatism react violently to horse serum and hemorrhage to death following "typhoid therapy" for chorea.

gated antigens in the animal. Fierz and his co-workers (24) have shown that sodium atoxyl-diazo-sulfo-anthranilate undergoes decomposition when injected into the guinea pig and couples with body protein to form the corresponding azo protein. The latter compound sensitizes the guinea pig. Furthermore, not only may antigenic substances be conjugated in the host but lethal substances may also be formed by a combination of bacterial products and animal tissues. This has been shown recently in a series of experiments by Firor and his associates (25). These investigators found that tetanus toxin is altered in the spinal cord into a lethal agent and that this product is not neutralized by tetanus antitoxin. We (26) have observed a precipitin reaction in rheumatic fever consisting of mutual precipitation of sera taken at different phases of the disease. Recent studies (unpublished) on the nature of the precipitin have shown that it is not absorbed by killed cultures of the organism obtained from the patient's throat at the time of pharyngitis. The precipitin is therefore not a primary antibody and is presumably evoked by some secondary antigenic substance. As suggested by Eagles and Bradley (27), the particulate matter in rheumatic exudates might play a similar rôle.

We have observed (28) that the spleen of patients with mild rheumatic activity contains some substance capable of evoking intense activity at a distant site. The nature of this substance is still unknown. However, recent work of Brokman (29) and his collaborators has shown that there is a complement fixing antigen in liver and spleen of patients dying with rheumatic fever. On one occasion we have been able to recover from rheumatic liver and spleen an antigen which fixed complement in the presence of fresh rheumatic fever sera. Extracts made in identical manner from liver and spleen of other diseases were inactive and sera from other diseases failed to fix complement with the antigen from rheumatic liver and spleen. It is our present concept that the liver and spleen of patients with active rheumatism contain an antigen to which certain cells of the R-E system have become sensitized. The release of this antigen into circulation therefore gives rise to an abnormal reaction of the sensitized cells.

IV. SUBJECTS FOR FURTHER STUDY

Before concluding, I should like to bring to your attention certain characteristics of the rheumatic process an explanation of which would clarify the disease problem.

First, we have already mentioned that hemolytic streptococcus infections which do not involve the respiratory tract or which give rise to suppuration rarely induce activity in a rheumatic subject. The simplest explanation is that severe or suppurative infections produce antigen in quantities too great to induce sensitization. However, just as skin sensitization (30) is most easily obtained from dermal application of an antigen, so too it may well be that endothelial sensitization is best elicited by action of the irritant on lymphoid tissue. The work of Dienes and Schoenheit (31, 32) has shown that the response to an antigen is altered by injecting it into infected tissue. Since he was able to produce a tuberculin-type of sensitivity to egg white by injecting this protein into a tuberculous focus, it seems to us that a reinfection of healed lymphoid tissue may enhance sensitization.

Second, the question arises: why then do not staphylococcus and pneumococcus throat infections induce rheumatic at-

tacks? This question is at present unanswerable; however, it is well known that hemolytic streptococcus is an excellent sensitizing agent. Is this because of its capacity to spread or its avidity for tissues? Is it because its exotoxins are vascular irritants or because the bacterial cell is rich in proteins? Is it because the lack of a thick capsule permits diffusion of small molecules from the cell or because it produces a sensitizing antigen not yet recognized? These are problems awaiting elucidation by the immunologist.

Third, there is a preferential distribution of rheumatic lesions in favor of the arterial side of the vascular tree. In 58 successive autopsies showing rheumatic auriculitis, we found only 2 that showed involvement of the right auricle and in these it was less severe than in the left auricle. The rheumatic process seems to be intensified in the presence of arterial blood. Whether oxygen tension is the significant factor in arterial blood is unknown.

Fourth, the administration of sulfanilamide in active rheumatism aggravates the disease (33). It will be of interest to find out whether this drug makes the body fluids more favorable to the rheumatic process or whether it takes an active part in the sequence of chemical events.

Fifth, when the patient with active rheumatism or the pregnant rheumatic subject contracts a fresh hemolytic streptococcal infection, one rarely observes any increase in the activity of the disease. Under these circumstances the antibody response to the new infectious agent usually follows a normal pattern. If the quiescent rheumatic subject can be induced to develop a normal antibody response to streptococcal pharyngitis, he should thereby be protected from rheumatism.

Sixth. Finally, there is the problem of the economic distribution of rheumatic fever. The prevalence of rheumatism among the poor is partly but not entirely attributable to their high incidence of upper respiratory diseases (34). Streptococcal pharyngitis is rarely followed by rheumatic fever in people maintaining high standards of living. For a number of reasons, which time will not permit me to discuss, we feel that these individuals may be protected from rheumatic fever by their diet. The relation of diet to the responses of the host, both specific and non-specific, is a matter of great concern to us, and is at present under investigation.

In conclusion, it is our belief that climatic, immunological, or dietary factors which modify the rheumatic immune response in the direction of normal will contribute to the eventual elimination of the rheumatic problem.

SUMMARY

This is our hypothesis:

1. Heredity and environment in combination produce an individual who does not handle respiratory infections with hemolytic streptococcus in a normal manner.

2. This abnormality is expressed as follows: the immune response to the primary infection is inadequate, with the result that viable organisms remain in inaccessible tissues after the healing of the primary focus.

3. The inadequacy of the immune response involves sensitization of the cells of the R-E system; that is, retention of antibody within them.

4. The surviving organisms release more antigen into the circulation.

5. Either the primary bacterial product or a secondary antigen is phagocytized by sensitized R-E cells.

6. Contact of this antigen and residual antibody within the R-E cells gives rise to an abnormal reaction.

7. This abnormal reaction stimulates the release of large quantities of globulin into the circulation.

8. At the same time an intense inflammatory reaction and striking changes in vascular permeability are induced in vicinal tissues.

9. The characteristic infiltration of wandering cells into the damaged tissues completes the evolution of the rheumatic lesion.

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Tumors in Cold-Blooded Animals; Their Significance in the Experimental Investigation of Cancer*†

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THE realization that cancers and other tumors are not diseases of man alone but are widely distributed among animals has been responsible for decisive progress in the field of cancer research. Further, it has come to be realized that no matter in what species of animal they occur, tumors having similar structure are much alike in their behavior. When these facts were demonstrated it became possible to study tumors by experimental methods, and justifiable inferences as to the nature of neoplasms in man could be drawn from study of the same kind of tumor in another species. Such studies in the past have dealt almost exclusively with tumors in warm-blooded animals, chiefly rodents and fowls. The more primitive cold-blooded vertebrates have been neglected because of the general belief that among them tumors are rare and consequently not readily available for investigation.

Our knowledge of tumors in cold-blooded vertebrates—in fish, amphibia and reptiles—has hitherto been based upon chance observation, and not upon the systematic study of a particular kind of tumor in a particular species of animal. It seemed desirable to search for tumors among these animals, for just as the cold-blooded vertebrates have been of great value in the physiological laboratory, so these simpler, less highly organized animals may be expected to prove favorable material for the investigation of problems of pathological growths, especially of cancer. This search has revealed a variety of tumors in all classes of cold-blooded vertebrates, tumors which are comparable in frequency to cancers in man. They have indeed proved very suitable for the investigation of several cancer problems.

I wish to present to you first, a brief account of several such tumors, and then tell you about our experimental studies. The tumors I have selected are tumors of the nerve sheath in marine fish, the snappers; carcinoma of the lip and buccal mucosa in a fresh-water fish, the catfish; adenocarcinoma of the kidney in an amphibian, the leopard frog; and papillary tumors of the skin and eye in a reptile, the green turtle.

Nerve sheath tumors (*neurilemmoma*, *neurofibroma*, *schwannoma*) *in fish of the snapper family* (*Lutianidae*). These tumors closely resemble the complex group of human neoplasms arising from the sheath of nerves. They occur in several members of the snapper family (grey snapper, dog snapper, school master),

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† From the Laboratory of Pathology of the School of Medicine, and the Biological Farm of the Wistar Institute, of the University of Pennsylvania.

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large subtropical and tropical fish much esteemed for food. The specimens were taken in the waters near the Dry Tortugas, a group of tiny coral islands in the Gulf of Mexico upon which the Carnegie Institution has maintained a Marine Biological Laboratory. These tumors arise in the corium or subcutaneous tissue, whence they project outward as flattened oval masses, stretching the epiderm to a delicate membrane devoid of scales. They vary in size from small nodules to conspicuous masses over 5 cms. in diameter. The total number of tumors which have been obtained to the present is 76. This relatively large number permits an analysis of the anatomical distribution and habits of the growths. It is found that most of the tumors are situated along the course of the larger subcutaneous nerves, particularly those of the head and the dorsal regions. Their peculiar distribution, together with their characteristic histological appearance, makes it very probable that these growths have their origin in the sheath of the nerves. They bear a striking similarity to tumors of the nerve sheath in man. Like them they form two main types, in one of which the component cells are oriented in such a manner as to form rows or so-called palisades; the other type has a very loose edematous structure, and no particular arrangement of its component cells is demonstrable. Also like nerve sheath tumors of man, certain of these tumors in fish become invasive and malignant. It is estimated that approximately 1 per cent of gray snappers (Lutianus griseus) are affected with this neoplasm; the incidence in the other varieties of snappers is not known.

Epithelioma of the lip and buccal mucosa in catfish (*Ameiurus nebulosus*). These tumors vary considerably in gross appearance. A common type is a flat nodular swelling of the lip or adjacent buccal mucosa of lighter color than the neighboring tissue. Another common type occurs as a round mass, quite pink in color, and often so large as to prevent closure of the mouth. Frequently more than one tumor is present. Whether these multiple tumors have arisen from several independent foci, or whether they represent dissemination from a single primary growth is as yet not known. It is especially interesting to observe that opposite a larger tumor on one lip there often is seen a smaller tumor on the other lip. This may possibly be an example of transmission by contact, or it may represent dissemination by the intercommunicating vessels of the mouth or even independent growth.

The histologic appearance of these tumors varies but little. Usually they have a papillary structure, i.e., groups of epithelial cells are supported by delicate strands of stroma. In some tumors the margin between neoplastic epithelium and neighboring tissue is well defined, and the tumor cells form compact masses which push downward as well as outward without apparent invasion. But in other tumors the compact grouping of cells is lost, the cells are loosely arranged, they invade and destroy tissue, they push into vessels and form emboli; such tumors are evidently malignant.

In general this tumor resembles the papillary form of human lip cancer, which also is usually slow to extend and has a long though malignant course.

Nearly 100 such catfish tumors have been obtained in one year from streams in New Jersey and Pennsylvania.

Adenocarcinoma of the kidney in the leopard frog (*Rana pipiens*). The general characteristics of these tumors, of which over 900 have been examined in

this laboratory during the past 7 years, are briefly as follows:

The tumors occur in one or both kidneys as solitary or multiple, white, solid or partially cystic growths varying in size from small nodules to large irregular masses several times the size of the kidney which they replace. The larger and presumably more rapidly growing tumors not uncommonly metastasize. Histologically, the majority of the tumors have the appearance of adenocarcinoma. The component epithelial cells are quite atypical and much larger and more basophilic than normal kidney cells; usually they are crowded in disorderly multiple layers around irregularly shaped gland-like acini. Numerous mitotic figures denote active proliferation; the stroma is scanty and poorly vascular; a capsule is lacking; and marginal extensions of the tumor infiltrate and destroy the adjacent kidney.

In a smaller group the component cells are less atypical, the tumor tubules are single layered and more orderly, there are few mitotic figures, and, while no capsule is present, no extension of the periphery occurs. A frequent variation from this adenomatous growth is cystic dilatations with papillary projections into the cyst.

All gradations are found between the frankly malignant, invasive, and destructive adenocarcinoma and the structurally benign adenoma, cystadenoma, and papillary cystadenoma. In general the larger tumors nearly always have a malignant appearance, though many minute nodules are also evidently carcinomatous. The neoplastic disease, once established, appears to be progressive, for tumors with evidence of recession such as atrophy, extensive necrosis, and marked overgrowth of stroma are uncommon.

The outstanding characteristic of the frog tumor is the frequent presence of acidophilic intranuclear inclusion bodies which in their general appearance are like those found in herpes and certain other diseases known to be due to viruses. They are invariably confined to the cells of the tumor and have never been observed in normal renal epithelium of tumor-bearing kidneys, nor in the cells of other organs. In their typical form they are conspicuous and readily recognizable, and in such form they are observed within most of the tumors. It is obvious that there must be developmental stages, and the appearance of the early stages is still a matter of doubt. Moreover there appear to be seasonal variations; at least the inclusions are more frequent in winter and spring than in summer and autumn.

The cancer of the frog is much more prevalent in the New England States and in the adjacent parts of Canada than in other regions.

Multiple papillomas of the skin and of the eye in the green turtle (*Chelonia mydas*). The neoplasms which have been observed in reptiles are even more limited in number than in amphibians and fish. Hence it is of particular interest to record that green turtles not infrequently suffer from papillomatous tumors which may attain so great a size as seriously to interfere with their locomotion, or which by involving the eyes blind the animals and render them helpless.

The tumors are located on the edges of the flippers, in the axillary regions, the neck, on the eyelids, the corneal surfaces, and on the tail. In shape they are hemispherical or globular, and have rough, warty surfaces covered with dry, coarse, cornified epiderm, which may become superficially ulcerated. Some of the tumors are sessile, others have a broad pedunculated base. In some areas, particularly in the axillary re-

gions, several are often crowded together; elsewhere they are solitary. In size, the individual tumors range from small warts a few millimeters in diameter to large masses 15 cms. across. All are of tough consistency, and have a dense white fibrous, bloodless cut surface.

Histologically, most of the neoplasms are typical papillomas, consisting of a fibrous core covered with many layers of epiderm, the surface of which has undergone extensive keratinization. All stages of the papillomatous growth are represented in the animal; the smaller show a preponderance of epithelial over mesodermal components; as the tumors increase in size the fibrous components become more prominent; in the largest growths they greatly predominate. Richly cellular areas, frequently encountered, indicate that the fibrous portions of the tumors are actively proliferating. Though most of the tumors observed appeared to be benign, in one animal at least they were cancerous, as indicated by widespread metastasis to the lungs.

The papillomas of the turtle correspond very closely to epidermal papillomas of man and other mammals, several of which have been shown to be caused by viruses. It would be of great interest if a similar etiologic factor could be demonstrated in these papillomas of a very different group of vertebrates.

Summary of the Occurrence of Tumors in Cold-Blooded Vertebrates

It has been shown that diverse kinds of cancer are of common occurrence in each of the several classes of cold-blooded vertebrates. The main significance of this fact lies in giving us a broader concept of cancer. Tumors are not diseases largely confined to man and the other more highly organized warm-blooded animals; they are equally common in the simpler, more primitive cold-blooded vertebrates; they are pathological phenomena distributed throughout all classes of the vertebrates.

Apart from the theoretical interest which tumors in cold-blooded vertebrates have, *we may now consider them as material for the experimental study of cancer.* For many biological investigations cold-blooded animals have decided advantages. As compared with warm-blooded animals, their various vital processes usually proceed at a much slower speed, they are much more dependent upon environmental factors; their tissues are much less vulnerable and have a longer survival period; in many forms the cells are much larger. These attributes permit a greater range in the experimental conditions than is possible with the higher and more complex animals.

The work I wish to report deals with the carcinoma of the frog; and in particular with the cause of this cancer, with the manner of its growth and with the modifying effect of temperature upon growth.

EXPERIMENTAL STUDIES ON THE CAUSE AND MANNER OF GROWTH OF FROG CARCINOMA

The cause of frog carcinoma. The experiments here reported all support the indication, first given by the frequent presence of intranuclear inclusions within the tumor cells, that the kidney tumor of leopard frogs is caused by a virus.

When inoculated as living fragments or cell suspensions into the lymph sacs, the cranial cavity, or the abdomen, the implanted material was resorbed and no significant local growth resulted. However, in over 20 per cent of the frogs surviving inoculation for more than 6 months, there developed in the kidney

tumors which were like the spontaneous neoplasms. The incidence far exceeded that in the controls. Inoculation of desiccated tumor and, in one group, of glycerinated tumor led to similar results; in somewhat over 20 per cent of frogs which survived for more than 6 months, renal tumors occurred. Evidently the tumor-inducing agent can resist conditions incompatible with the viability of animal cells. Attempts to transmit the tumor to alien species proved unsuccessful. These results can best be interpreted as indicating the existence in the inoculated material of an organ-specific carcinogenic agent having the attributes of a virus.

That certain viruses induce neoplastic proliferation is a well established fact. The problem of the etiologic relation of viruses to tumors and the nature of virus-induced tumors have been so recently and fully reviewed by Andrewes and by Rous, that no further discussion is necessary here. But, it is worthy of emphasis that such tumors have proven to be true neoplasms, that several varieties of them are known to exist, and that they are not confined to one particular class of animals. The kidney tumor of frogs, which is carcinomatous in character, would appear to be another example.

The manner of growth of frog carcinoma, studied by direct microscopic examination of living intraocular transplants. The characteristics of cancer growth have hitherto been studied chiefly by histologic method, that is, in fixed, sectioned, and stained material. But study of neoplastic growth, like that of normal growth, involves the study of something alive and continuously changing, of something dynamic, not static. Neither the dynamics nor the mechanics of growth can be investigated by histologic methods. Rather, growth should be studied by a method which permits continuous observation of the living tumor. The method we have adopted is to transplant small pieces of tumors into the anterior chamber of the eye, where they soon establish themselves. Here, details of form as well as arrangement of constituent cells can be observed directly through the thin transparent cornea by means of the microscope, and be recorded by photographs from the earliest to the most advanced stages. There is at present no other method which permits as continuous observation of living tumor, and which gives as vivid and as objective a picture of its manner of growth and progress.*

The tumors which furnished the transplants were typical large invasive adenocarcinomas having the usual irregular and apparently anarchic arrangement of their component tubules and acini. However, the transplanted tumors developed according to definite and well-defined structural patterns, their type depending on the immediate physical environment. Three such morphogenetic patterns were observed.

Unimpeded outgrowths into the aqueous humor characteristically assumed a tubulo-papillary arrangement; the earliest formation consisted of solid, purely epithelial cylinders, many of which at later stages acquired a lumen and thus became tubular; generally only the coarser projections developed vascular stalks. Further growth was made by repeated dichotomous branching and lateral outpouching of the tubules. Where the tumor grew in contact with firm, even surfaces, such as lens or cornea,

* In these experiments I have enjoyed the collaboration of Dr. H. Schlumberger, a member of our department. We both wish to express our appreciation to Mrs. M. R. Barrett for her interest in developing the photographic technique.

differentiation was lost and broad membranes formed which gradually spread over the surfaces; secondarily, new cylindrical or tubular processes arose from such indifferent cellular carpets. Where the tumor made contact with loose tissue such as iris, it invaded this organ, and, supported by the stroma, assumed an acinar pattern quite like that of the original adenocarcinoma of the kidney. All three types of growth were sometimes found coexisting in different portions of the anterior chamber.

The mechanics of growth and development of normal tissues are now fairly well understood, but we have no such understanding of the mechanics of growth and development of neoplasms. Lacking this information, it has been customary to speak loosely of the "lawless" growth of cancer.

However, it appears from the present experiments that there are quite definite patterns of growth of cancer, the type of which is determined by the immediate physical environment. Evidently cancers are responsive to laws that govern growth and organization, and a step in the analysis of these laws has been made in the present investigation.

Characteristics of frog carcinoma in tissue culture. We now come to a second method which permits further analysis of the mechanism of growth, namely, growth in tissue culture.

Tissue culture has much in common with the method of implanting tissues in the anterior chamber of the eye. In both cases, the tissue is placed in a clear medium which is confined within a transparent chamber; the nutrition and metabolic exchange of the implant is carried out, during the earlier stages at least, solely by diffusion, that is to say, without a blood supply; both methods permit direct and continuous microscopic observation of living tissue, but each has certain advantages which render it complementary to the other.

The present study is concerned with characteristics of frog carcinoma in tissue culture. The experiments afford an opportunity to compare growth and organization of the same tumor in vitro and in vivo, and, further, to compare a malignant amphibian cell with malignant cells in general.

It was found that the adenocarcinoma of leopard frogs may be cultivated with ease in plasma media. In such cultures two types of growth occur with regularity. The first is in the form of tubules which promptly grow out in the solid medium and retain their tubular form as long as they remain completely enveloped by plasma. When, however, they make contact with the surface of the glass, they adhere to it, the part in contact becomes flat, and its cells now grow no longer as tubules but as membranes.

The manner of growth in vitro resembles the growth of transplants of the same tumor in the anterior chamber of the living eye, thus suggesting that in each case the habit of growth is determined by the same morphogenetic factors, i.e., those inherent in the cells themselves, and those depending on interfacial forces.

The malignant cells of the frog carcinoma have the characteristics which in general distinguish malignant cells from normal cells of corresponding type. In comparison with adult kidney cells, their normal homologues, the conspicuous properties of frog carcinoma cells are: larger and more variable size and shape of cell body, of nucleus, and nucleolus; coarser and denser structure of cytoplasm, of nucleoplasm, and of nuclear membrane; increase in number of mito-

chondria, and more frequent occurrence of mitosis. These cytological characteristics remain unaltered in cultures maintained for as long as six months.

Frog carcinoma is a transmissible disease due to an agent which induces inclusion bodies, and which has other attributes indicating that it is a virus. The general correspondence in character between its cells and the malignant cells of mammalian tumors of diverse origin suggests that neoplastic phenomena are essentially alike, no matter in what group of animals they occur or what their causal factors may be.

Effect of temperature on growth of frog carcinoma. In the preceding sections it has been shown that the manner of growth of a cancer is profoundly affected by its immediate physical environment. Another environmental factor which may affect the growth of cancer is temperature.

For studying the effect of temperature on growth of tumors, the frog carcinoma is particularly good material. Since the temperature of the frog is practically that of the environment, we have an opportunity to investigate the effects of temperature over a far wider range than is possible in warm-blooded animals. Moreover, the frog carcinoma is easily established in the anterior chamber of the eye, where its growth may be observed with the microscope from the earliest to advanced stages.

In normal tissue it is an established fact that growth and development is influenced by temperature not only quantitatively but qualitatively.

In tumors, does temperature also affect the velocity of growth? Does it affect the ultimate size attained? Does it alter the character of the growth? These are the questions with which we are concerned.

In the first series of experiments, frogs, immediately after being inoculated, were transferred to a constant temperature room at 7°C., control groups being kept in the vivarium at 22°C. They were observed for 2 to 9 months and during this time they received no food, since frogs at the lower temperature will not eat. It was found that tumors were able to establish themselves and develop at both temperatures, though the proportion which became established was somewhat less at 7° than at 22°C. The main difference was in the rate of growth, this being slower at the lower temperature. A further difference was the earlier and more effective vascularization of the implanted tumors in the control group at 22°; this, in turn, led to more massive tumor growth. In the second group of experiments, the effect of temperature was studied on tumors that had already become established. Following inoculation, frogs were kept in the vivarium for 2 or 3 weeks. Those with growing tumors were then transferred to constant temperature rooms at 7° and 28°C., respectively.* These differences in temperature were considerably greater than those of the first series, and the effects of temperature became more strikingly evident. In both groups, growth of tumors continued, again at a slower rate at the lower temperature. However, there was little difference in the size of tumor which was finally attained, for though the initial rate of growth was greater at the higher temperature, growth retarding factors also came into play much sooner. Thus, regression of tumors developed in a greater proportion at 28°C. than at the lower temperature.

* These temperatures were chosen because they represent the extremes at which frogs can be maintained and continuously observed for long periods of time.

In the next group, the effects of temperature upon well established, large, vascularized tumors were investigated. When frogs with such tumors were transferred from the vivarium to the cold room, growth of tumors continued, but at a slower rate.

Next, tumors which had attained large size at 28°C., were removed, divided into small pieces and retransplanted. The frogs immediately afterwards were placed into constant temperature rooms at 7° and 28°C. The retransplanted tumors grew at both temperatures; the effects of temperature were the same as on the parent growth. These experiments showed that prolonged growth of a tumor at one temperature did not alter its essential character.

In a final group of experiments, the effects of natural hibernation were studied. After inoculation, frogs were transferred to suitable cages in a pool just before ice formed on the surface. The frogs remained submerged in a condition of hibernation for 10 weeks during which the ice persisted and the frogs remained at approximately 4°C. They were then removed and examined. Practically all of the implanted tumors appeared in good viable condition as evidenced by their translucent appearance; in a few, small tubular buds had formed. The animals were now placed in the vivarium at 20°, at which temperature active growth soon began and continued at average rate. The long period of dormancy at 4°C. consequently did not prevent growth of tumors when the animals were returned to a temperature more favorable to growth.

The general conclusion to be drawn from these experiments is that a low temperature, such as 7°C., does not arrest nor change the mode of growth of frog carcinoma transplanted to the anterior chamber; it does, however, reduce the velocity of growth, possibly by preventing early vascularization. High temperature, 28° C., while increasing velocity of growth, also tends to lead to its earlier decline and to retrogression of the tumors. These effects are similar to the effects of temperature upon growth and devlopment of normal tissue.

It is well known that transplanted tumors, like normal tissues, have a definite cycle of growth. After a period of slow growth comes one of rapid increase in size. This is followed by gradual decline in the rate until growth may stop entirely, and finally the tumor may regress. The whole cycle proceeds faster at high temperatures than at low. Thus in another respect the growth of tumors is found to be qualitatively similar to that of normal tissues.

General Summary

In the first part of my lecture I have presented to you types of cancers which are common in each of the 3 classes of cold-blooded vertebrates and shown their close similarity to corresponding tumors in man. We may consequently regard neoplastic growth as a pathologic phenomenon common to *all* classes of vertebrates. This concept widens the scope of our inquiry into the nature of neoplasia, and more varied material has thereby become available for cancer research.

The second part of my lecture dealt with experimental studies on a cancer in frogs, a typical invasive and metastasizing adenocarcinoma. Evidence has been presented that this cancer is caused by a virus. Thus in an amphibian, a virus has been shown to be capable of producing a malignant tumor. Since viruses are known to cause certain tumors

of birds and mammals, it appears that they are a frequent cause of tumors throughout the animal kingdom. Whether in man any cancers are caused by viruses is yet to be learned.

The mechanics of growth of this cancer have been investigated by a method which permits direct and continued microscopic examination of the living and developing tumor. It has been learned that the manner of growth of this cancer is largely governed by physical factors. Neoplastic growth is not lawless. Lastly, we have studied the effect of temperature. It has been found that temperature affects cancerous growth in much the same way as it effects growth of normal tissues. Thus it has been possible from study of tumors in cold-blooded animals to gain information on the causes and laws of growth of neoplasms.

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The Diagnosis of Human Cancer*

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CANCER is a morbid process characterized by excessive vegetative activity of epithelial cells whose numbers soon cause them to escape from their normal boundaries and more or less completely lose their characteristic morphology, so that their normal relationships to one another and to the tissue in which they are supported is no longer maintained. They then proceed to insinuate themselves between and among the cellular and intercellular elements of their parent tissue and of the adjacent tissues, with resulting separations and compressions that are soon followed by necrosis, ulceration, hemorrhage and secondary infection. Early in some cases, late in others, there is apt to be invasion of new territory by progressive local infiltration, by permeation or by metastasis, so that from one primary tumor there may originate others and sometimes innumerable secondary tumors, whose progressive enlargement occasions atrophies, obstructions and compressions by which the life of the victim is made miserable and finally terminated.

At least a million people, in this country, are afflicted with some variety of this tumor, in some stage of development, and every year approximately one hundred and fifty thousand of them die of it, while many more who suffer from its early stages or milder varieties die of other diseases before its symptoms are manifested.

Its inception is slow, unobtrustive and painless so that it is usually well established when discovered. This is one of its most distressing peculiarities, as it postpones treatment until complete eradication of the tumor tissue can no longer be effected. Nothing seems to be more reasonable than the prevalent belief that, no matter whether attacked by the knife, the cautery, the caustic, the concentrated rays of the sun, x-rays or radium, it ought to be more easy to eradicate or destroy a minute local lesion than a large distributed one.

Though a single morbid process, cancer is not a single disease in the clinical sense. There is no resemblance between cancer of the skin with its visible destructive ulcerations, cancer of the breast with a hard painless "lump" in the soft mamma, cancer of the stomach with persistent indigestion and increasing vomiting, and cancer of the lung with cough, expectoration and hemorrhages, yet all are but different clinical manifestations of the same process. For each there are clinical symptoms and for each there are clinical methods of diagnosis that sooner or later lead to the suspicion of cancer, and it is to the laboratory that the clinician eventually turns for the answer.

The patient's chief hope of benefit is in his physician's ability to find the cancer before it shows itself to be cancer. To that end, for more than a quarter of a century, an extensive campaign has been carried on, the purpose of which has been to impress the public with the necessity

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of the early discovery of the disease and they have been advised to subject themselves to semi-annual physical examinations by which unsuspected lesions might be discovered. Some impression has been made, yet it remains the daily experience of those who work in cancer clinics that patients still appear with massive lesions, excusing themselves with the statement "it never bothered me at all".

Some have, however, profited by the instruction, and are periodically examined. Small lesions are thus frequently discovered and treated, and whether we believe that they are *cured* or not, the patients are immensely benefited, their comfort and their lives being greatly prolonged. There are naturally some persons who become frightened and in undue apprehension present themselves with a variety of trifling lesions of doubtful nature for which they desire and receive treatment. These may be all right, and many may be cured of whatever it was that frightened them, but unless the operator be sincere and thorough, these cases may later be counted as cancers that were cured, when they were not cancer and the patients in no danger of getting it.

Some surgeons, roentgenologists, and radiologists declare their interest to be in the patient. It makes no difference to them whether a lesion be cancer or only resemble it; they treat it just the same and try to get it well. If it disappears, that is to the patients good and what does anything else matter? I am not opposed to that principle; it probably does not matter one way or the other unless they attempt to make scientific deductions or supply statistical information from observations made from such slip-shod methods. If one treat a hundred patients, some of whom had cancer, while others did not, and if some of them get well, how can he tell whether many or any of those who recovered ever had cancer?

In many of the infectious diseases it is possible to arrive at a correct diagnosis through the discovery of the specific microörganism of that disease in the lesion, no matter how small it is. But in cancer it is impossible because there is no known specific microörganism. Even the possibility that cancer is a virus infection carries with it no probability that this means of diagnosis will be applicable because of the invisibility of the viruses and their biological peculiarities.

It has been suggested that cancer is but the local manifestation of a constitutional disturbance and that efforts should be directed toward finding the nature of that disturbance. If it were found, it might be possible to discover predisposition to cancer before it developed, and so do something to prevent its development, or, failing in that, to mitigate or cure it.

This field has been explored from every point of view at our disposal but no one has been able to show that any biochemical condition of the patient with early cancer manifests any constant deviation from the normal. It has also been suggested that the growth of the cancer may be attended by the extraction from the body juices, or the addition to them, of some abnormal metabolic product present in very small quantities at first, but increasing with the growth of the tumor until its accumulation in the later stages of the disease may be partly or even solely responsible for the cachexia preceding death. The demonstration of such a factor in the body juices might be

of great diagnostic value, but nothing of the kind has been discovered.

The immunity reactions have not been neglected. Antigens have been prepared from cancer cells, and from embryonal cells on the supposition that the cancer cells shared the qualities of embryonal cells, and attempts have been made to bring about specific precipitates in test-tubes, or to obtain allergic phenomena by injecting the antigen into or under the skin. The blood coagulation time, the erythrocytic sedimentation time and the varying viscosity of the blood plasma and serum have been studied without avail.

In closing this hasty synopsis of the search for new diagnostic procedures it is, however, necessary to say that only a very few of the methods seemed promising and that, thus far, the best of them is not dependable within about 20% of error.

We are, therefore, left with the lesion itself as the only factor from which the certain diagnosis of the disease may be achieved. The method of investigating the lesion must vary in different cases accordingly as it is:

1. Visible and accessible;
2. Invisible but easy of access;
3. Invisible and difficult of access.

1. *The Suspected Lesion Is Visible and Accessible:* The term visibility is not limited to that which can be seen with the eye alone, but includes all those that can be seen with the aid of the necessary instruments such as the otoscope, ophthalmoscope, rhinoscope, laryngoscope, bronchoscope, gastroscope, proctoscope, cystoscope and speculum. With the aid of these instruments it is possible visually to examine hidden lesions in a manner comparable to those of the skin. It would be extremely difficult to obtain accurate figures upon this matter, but inasmuch as the cancerous lesion is usually fairly well established when relief for it is sought, and as those who use these instruments are skilled in their employment, it is probable that a correct diagnosis can be reached by simple inspection in about 75% of the cases. In superficial and early lesions of squamous-covered epithelial surfaces, especially the cervix uteri, assistance in the diagnosis of cancer in suspicious cases may be obtained by Schiller's method of painting the surface with Lugol's solution, which colors the normal tissue yellow, but leaves the cancer tissue unchanged. The exact value of this method is, however, debatable.

Because a lesion is visible does not mean that it should not be palpated when that is possible, for the tissue of most cancers is firmer than normal tissue of the same region, and the palpating finger is also able approximately to determine the extent of the basal infiltration. Those who treat cancer, by whatever method, should school themselves in both the visible and palpable characteristics of the lesions they aim to benefit.

2. *Lesions That Are Not Visible But Are Easy of Access:* Chief among these are the lesions of the breast and the testis. A lump in the breast when sufficiently superficial and free may be pressed upward toward the skin so that its general form and size can be made out.

About 75% of all the tumors of the breast are cancers; one has a three-fourths chance in favor of any "lump" in the breast being that tumor. It is, however, the remaining fourth of the cases that are puzzling, especially when they are small and, as not infrequently the case, moveable, and especially when the patient is young. One must not forget that a woman's bosom is one of her charms, and that a mistake in diagnosis

in the case of a young and handsome woman may entail dire consequences. What consequences depend upon the hands into which she falls. One surgeon may insist upon a radical amputation of the breast, another will be content with a simple mastectomy, a third may try excising the lump or a fourth prescribe a long course of x-ray treatments. In any event there will be suffering, loss of time, and expense, which though serious in themselves are followed by profound mental depression that inevitably results from the beauty-destroying mutilation, the diminution of matrimonial opportunity, the depressing sense of inferiority and the harassing dread of the recurrence of the disease. Women are brave and disguise these feelings, but they suffer just the same.

To escape the infliction of these evils every attempt should be made to attain the correct diagnosis. We should call upon every available adjunct—thorough inspection, careful palpation, transillumination, x-ray plates, and occasionally, though rarely, lipiodal duct injection followed by x-ray plates. But the shortest cut to the correct diagnosis, and the most certain means of attaining to it, is by the biopsy examination about which more is to be said later.

The enlargements of the testes fall into the same category. It may be possible to achieve the correct diagnosis of the enlargement without it, but it is very easy to open the scrotum and examine the organ directly, and no harm is done, for if not cancer, the chances are that it is tuberculosis or some other condition for which orchidectomy is the appropriate treatment and for which the exploratory operation prepares the way. The mental effect of the operation upon a man in no way compares with the result of mastectomy in a young woman.

3. *Lesions That Are Both Invisible and Inaccessible:* There scarcely remains any portion of the anatomy inaccessible to the modern surgeon. What is meant, however, is that the invisible lesion is uncertain in its location, and only accessible through some major surgical operation such as might willingly be undertaken for treatment, though with reluctance for diagnosis.

Here aid must be sought from chemistry and roentgenology. The former when the lesion is supposed to be in the stomach, the latter in all cases of suspected alimentary tract lesions.

The new flexible gastroscope promises to be of great aid in the diagnosis of cancer of the stomach, and is being employed for that purpose in the Philadelphia General Hospital in all suspected cases of gastric and intestinal cancers, but the x-ray examination after the barium meal, both with the fluoroscope and the x-ray film, is invaluable and very dependable.

When these methods are inapplicable, as in suspected cancer of the liver, pancreas or ovaries, the exploratory laparotomy is the only means of diagnosis, though only in the case of the diseased ovaries is much benefit to be expected from the discovery of the disease in an organ that cannot be removed or from which there is little probability that the discovered cancer can be eradicated.

Not infrequently the same difficulty is met that attends all cases in which the diagnosis is to be made by the eye and finger. The diseased organ is, indeed, exposed and the lesion is discovered, but to find out whether it is cancer or not it may be necessary to appeal to the laboratory and to the microscope.

The microscope is not a mechanical apparatus whose results are mathematically attained and infallible—as,

for example, are those of a correctly manipulated adding machine. It is nothing but an optical amplifier. It tells nothing! It only increases the size of the objects examined so that invisible details of structure can be made to contribute to the sum total from which the diagnostic interpretation is to be made. Its value is in proportion to the knowledge and experience of the user. It is not the microscope that makes the diagnosis, but the man who looks into it. Moreover, the microscope only shows what is placed beneath its lenses, and if that consists of material badly chosen, or improperly prepared, the result of the examination may be confusing and the deduction erroneous. There are occasional close resemblances between things whose nature is otherwise very dissimilar; there are differences of opinion, in the minds of capable men, as to the interpretation to be placed upon certain factors; there are differences in the methods of approaching the same object of study, so that it not infrequently happens that different conclusions will be arrived at by different competent pathologists.

I have heard it said—as though true in all cases—that one may get a different diagnosis of a tumor from every pathologist who examines it. I doubt whether that is ever true, but it is sometimes possible to receive what seem to be ridiculously divergent opinions about the same tumor from two or three thoroughly capable, experienced, well-informed and sincere men. Of several thousand tumors, sections of which are in my private collection of microscopic slides, there are about sixty that have never been satisfactorily identified, although they have been studied by many pathologists, some of whom are among the most noted in the country.

There are tumors that the pathologist may correctly diagnose by a glance of the eye, others by the eye supplemented by the finger. Others may require a hastily made (frozen) microscopic section. But there are still others the identification of which will require the best skill of a technician and the aid of special apparatus and special methods of staining.

Let everyone realize that pathological diagnosis is as difficult as clinical diagnosis, and there will be fewer disappointments. The pathologist should always be furnished with all of the information contained in a carefully taken protocol. His work is difficult and no one should sneer at him if at the end of his resources, he "cannot be sure" whether a piece of tumor tissue sent to him is to be regarded as "malignant" or not. In 95% of the cases he may have no trouble, but in the remaining 5% he will, if careful, find it necessary to reserve his opinion and only say "suspicious" or "to be carefully watched".

All this is in anticipation of the final and supposedly infallible means of diagnosis, the biopsy.

BIOPSIES

A biopsy is the microscopic study of a piece of tissue, usually from a tumor, removed in order that it may be so examined.

There are some extremely fundamental and important facts for those who take "biopsies" to keep in mind, lest the purpose be defeated and confusion instead of clarification result:

1. The tissue must be taken from a characteristic part *of the tumor.*
2. It should be large enough to permit of satisfactory examination—the larger the better.
3. It should be of such a shape or so marked that it can be properly oriented and cut.

4. It should include some of the adjacent tissue, so that it will be possible for the pathologist to learn the relations of the two where they abut.

1. *The Tissue Must Be Taken from a Characteristic Part of the Tumor:* Superficial malignant tumors frequently have vegetations or ulcerations of the surface. If the biopsy material be so taken as to show one or the other of these and nothing more, the erroneous conclusion is reached, in the first case, that the tumor is a wart, or in the second, that it is simply inflammation. A fragment having a greater depth might in either case have shown the downward growths of epithelium indicative of a malignant tumor. The fragment must, therefore, descend deeply below the surface.

Tissue excised from the margins of ulcerated lesions should always be cut long enough to include part of the ulcer on one side and of the normal tissue on the other. The epithelium at the margin is frequently so disturbed by inflammatory hyperemia, edema and cellular infiltration that it is difficult to decide whether the activities are primarily in the epithelium and constitute a tumor, or secondary in the epithelium and only the result of inflammation. The resemblance that the margins of ulcers often bear to cancer has led to many errors of diagnosis. The conservative observer inclines to view the lesion as inflammation, the more radical is certain that it is tumor.

These matters do not apply to most of the deeper tumors, but in obtaining the biopsy material from them, care should be taken to see that the tissue represents not only the substance of the tumor, but some part of it not in an advanced state of necrosis, degeneration, hemorrhage or infection. This should not be difficult when the biopsy material is taken with the knife, but is impossible when it is secured with a needle and the operator can only surmise into what it is penetrating.

2. *The Tissue Fragment Should Be Large Enough to Permit of Satisfactory Examination:* When the suspicious lesion is small and superficial, it may be advisable to excise it completely for biopsy. If the patient subsequently complains that all has been removed, when permission was given for the removal of a small piece only, there should be little difficulty in placating him by explaining that the lesion having been found to be very small, it seemed wise to remove it at once, rather than to perform another operation later.

It is always a joy to the pathologist to receive and study an entire small tumor, instead of the small fragments he usually receives. In simple cases of common tumors, it may be possible to make the diagnosis from the examination of a very small piece, but so soon as the least complication arises, the desirability of a larger piece is needed when it can no longer be obtained. When possible, take a sufficiently large piece of tissue to begin with.

In a general way, the smaller the fragment of tissue obtained, the less can be learned from it; and the larger it is, the more certainly may it fulfil its purpose. The judgment of the operator will prevent the taking of a biopsy from becoming a source of mutilation and disfigurement.

From an eye-lid or from the wing of the nose no one would think of taking a centimetre cube of tissue, though more than that might with advantage be taken from an exposed lump in the breast.

From superficial lesions a block of tissue measuring about 5 x $2\frac{1}{2}$ x $2\frac{1}{2}$ mm. is appropriate; from deep lesions 20 x

20 x 10 mm. may be obtained with advantage.

3. *The Biopsy Material Should Be of Such a Shape Or So Marked That It Can Be Properly Oriented When Sectioned:* The fragment of tissue removed for examination frequently proves to be without shape and without relationship and thus extremely puzzling to the technician who has to prepare it for the pathologist. It is very provoking to find the sections cut in a wrong plane. This naturally applies most particularly to fragments of tissue taken from a surface, as these must always be sectioned *perpendicularly* to the surface. Some method of marking the direction is therefore desirable and can easily be accomplished by thrusting a small pin through the tissue, from the surface downward at the time that it is taken. Through horizontal or tangential sections, where vertical cuts are necessary, deceptive appearances may be produced so that nothing can be learned from material obtained with difficulty but spoiled in the preparation.

4. *The Biopsy Should Include Some of the Adjacent Normal Tissue Whenever Possible:* The fact that the study of the margin of a malignant tumor (not of an ulceration upon the tumor, however) may enable its method of invading the adjacent tissue to be observed, has already been pointed out, but a generous allowance of the normal tissue against which the tumor abuts or into which it extends, may be valuable to the pathologist for other reasons.

The usefulness of such tissue is nowhere better exemplified than in deciding upon the benignancy or malignancy of the circumscribed and encapsulated tumors (adenomas) of the mammary gland. Only within recent years has it become generally recognized that the mammary parenchyma, as the endometrium, is subject to remarkable evolutional and involutional modification as it is played upon by the endocrines active at the menstrual periods and during pregnancy. Unless the histopathologist is acquainted with these periodic structural alterations, serious blunders in diagnosis are inevitable.

The tumors of the mammary gland, both benign and malignant, are composed of or descended from mammary epithelium, and, until anaplasia completely transforms them, their cells are subject to the same stimuli and in much the same manner as the cells in the normal gland. Ignorance of this fact has occasionally caused perfectly benign tumors (periductal fibromas) to be described as showing "carcinomatous change" when only normal menstrual or pregnancy glandular hyperplasia was present. As one error often leads to others, this mistake has led to the conclusion that benign periductal fibromas, or adeno-fibromas, frequently become carcinomas, and that sudden increase in the size of a small tumor whose presence in the breast has been recognized for years, indicates "malignant change".

It is stated in book after book that cancerous degeneration (change) in the benign tumors is common, although evidence by which to prove it scarcely exists. A famous case was reported for the express purpose of proving such malignant change in a periductal fibroma had taken place. In the same breast a periductal fibroma and a cancer were found intimately associated. The writer deduced that the former having undergone malignant degeneration, the cancer was escaping through the capsule and infiltrating the breast. When I studied the case, I found that the cancer was about equally divided between the tumor and the breast, but that there was just

as good reason for supposing that the cancer arose in the breast and invaded the adenoma as the reverse. Indeed, as cancer of the breast is so common independently of adenomas and so regularly infiltrates the adjacent connective tissues, it would seem to be more natural that the invasion of the adjacent benign tumor was but a circumstance in the general invasive growth of that cancer.

During pregnancy the growth of the mamma is slow and depends upon the replacement of its adipose and connective tissues by the increasing glandular parenchyma. If there be a periductal fibroma in the breast at the time, its parenchyma grows *pari passu* with the breast and its increase in size may attract little attention. But sometimes, after the birth of the offspring, when the breast rapidly swells, with the beginning of lactation, the tumor may also suddenly and considerably enlarge for the same reason. The tumor secretes like the breast and swells for that reason.

A two-fold increase in the size of such a tumor may arouse such anxiety as to lead the surgeon to excise the tumor, to perform mastectomy, or even radically to amputate the breast at a time when it is most needed, and no real danger menaces the patient.

It should now be evident why it is so desirable to have breast tissue as well as tumor tissue so as to control the microscopic appearances shown by the one with those shown by the other. Each reflects the state of the other. If the tumor is of the type ordinarily called intracanalicular, with a few duct-like elements stretched over polypoid myxofibromatous stroma, the adjacent normal mammary tissue will usually be found to be in the *resting stage* and its epithelial elements to consist mostly of ducts. If, however, the mammary structure is evolving as is shown by increased size of the cells, hyperchromatic condition of the nuclei, occasional mitoses, formation of acini, or the appearance of lobules, the tumor tissue will show parallel activity. There will be irregular accumulations of epithelial cells filling the ducts, which become numerous; the polypoid intracanalicular formations disappear and glandular acini may become numerous. The tumor ceases any longer to be "intracanalicular"; it becomes racemose. In some cases the whole of the tumor is changed into an enormous, dense cluster of acini, and transformed into a "simple adenoma". With the termination of the secretory phenomena and the end of lactation, the tumor, as the breast, undergoes involution and slowly returns to its simple adeno-fibromatous appearance. Similar though less striking changes occur in both breast and tumor at the menstrual cycles, when the comparison of the one with the other may explain the suspicious appearances shown by the tumor.

In mammary cancer occurring before the climacteric, the occurrence of menstruation with its temporary mammary hyperplasia also modifies the histological picture of the carcinoma, increasing the parenchyma and intensifying its glandular pattern through the temporary appearance of acini throughout the tumor. During the menstrual hypertrophy it may appear as an "adeno-carcinoma" (gland-like pattern), in the intervals between the periods, as a scirrhus. But cancer of the breast usually occurs after the menopause and so escapes the described phenomena. However, after the menopause the breast may be subjected to stimulation, constant or intermittent, resulting from hormones whose presence in the blood depends upon pathological conditions in other organs. Under these

conditions the parenchyma of the breast may show no rhythmical evolutions and involutions, but a confusion of the results of both taking place simultaneously, and producing pictures resembling those seen in carcinoma and often mistaken for it (chronic cystic mastitis).

The next matter for consideration is the means by which the material for biopsy study is to be obtained. The operation, done under local anesthesia in most cases, may be performed to best advantage with a small sharp knife and a pair of forceps. As the tissue fragment is small at best, extreme care should be exercised neither to crush it with the knife or forceps. Crushing and squeezing the tissue sometimes results in dislocating the single cells or groups of cells from one position to another with resulting unnatural and puzzling appearances.

The operation may also be performed with an electric knife or a wire loop. These are probably less appropriate for the removal of very small fragments of tissue as they are apt to cook its edges, after which an inexperienced observer may be surprised to see cuboidal epithelial cells transforming by imperceptible graduations into elongated spindles with rod-shaped nuclei. Such overheated edges must be overlooked in reading the section and only the deeper, unaltered parts of the sections studied.

When the lesion is situated in the rectum, larynx, uterus or other less approachable position, the punch biopsy forceps or the Noble forceps may be used. The instruments should always be very sharp and cutting, however, and crushing must be avoided. For still more deeply seated lesions, such as tumors of the breast, the tissue fragment is frequently obtained by means of a hollow needle, or one of the various small canulas and harpoons expressly made for the purpose. These all furnish extremely minute fragments of tissue, difficult to handle and to orient. Sometimes they fulfill every expectation and the diagnosis can be made without hesitation, but they often fail to contain the essential tissues in condition to be identified. Let it not be forgotten that the larger the fragment, the more useful it will be.

Related to the biopsy method is diagnosis by the extraction of fluid from the chest, the peritoneal cavity or from a cyst, with an aspirating needle or an ordinary hypodermic needle. The fluid may then be centrifuged and the cells collected in the sediment, spread upon the slide, fixed and stained, or as is probably better, the supernatant fluid is decanted and replaced by a fixing fluid. The fixed sediment is then treated as a tissue, embedded in paraffin, cut, stained and mounted. It may be possible to achieve the diagnosis when abnormal cells found in the sediment can be identified; impossible when they cannot. The chief difficulty is that the cells are without relation to other tissue elements.

It is sometimes asked whether the taking of biopsy material may not be injurious in that it disturbs tissue tension so that tumor cells may escape into a new environment, connects the tumor substance with the surface so that there may be accelerated growth and fungation, and brings about an opportunity for hemorrhage and infection.

Any of these evils may result, but they are very rare in the experience of those accustomed to observing and handling malignant tumors.

It may be bad practice to open the capsule of a tumor, but that need not be done because of the ease with which

whole small tumors may be removed. In cases in which lymph-nodes are under suspicion and it is uncertain whether the disease be secondary carcinoma, lympho-sarcoma or Hodgkin's disease, no incision into the nodes should be made, but a whole isolated node or a whole cluster of nodes removed.

When one considers the constant movements and manipulations that most tumors undergo in the daily life of the patient, the frequently forcible manipulations made by the examining doctor, it seems as though the taking of the biopsy might not be a serious matter.

When the tissue for biopsy has finally been secured, what shall be done with it? The answer to this question is unequivocal. It must be treated so that it shall not deteriorate by drying or solution or contraction. It is best to immerse it immediately in some preserving fluid in which it cannot deteriorate while awaiting further treatment. How vexatious it is to find that after great pains have been taken to secure the appropriate tissue, it has been rendered useless by being carelessly permitted to dry upon a piece of gauze before ever it reach the laboratory! A supply of bottles containing the preservative should always be available to the surgeon. The details of preservation and treatment are not proper subjects for discussion here. They are rather a matter of mutual agreement and regular routine between the surgeon and the pathologist. The preparation of the tissue for study may differ with the urgency of the case.

If an immediate diagnosis is asked for, and the patient is being kept under anesthesia, awaiting the diagnosis upon which an operation is or is not to be performed, or is to be performed one way or another according to the verdict, the tissue for biopsy, carefully protected from deterioration by drying, may be sent to the laboratory and be frozen with carbon dioxide gas, hastily put through some special method of staining and the examination completed in from 10 to 30 minutes. Frozen sections are not much employed in Philadelphia, except in those cases in which the diagnosis, as has been suggested, modifies the operative procedure already under way. The reasons are various. First, there is the undue bustle and hurry that causes the pathologist to be hasty in his judgment. The patient and surgeon are waiting and a diagnosis must be made! In some other cities, as Buffalo, it is practically the only method of section cutting now in use. I have seen both beautiful and large sections so prepared, but in Philadelphia the paraffin method is generally preferred, and whenever possible the tissue is so prepared, the results seeming to be more satisfactory.

There are other things about the frozen section method to which attention should be called. Unless it is frequently employed by one skilled in its performance, it is apt to fail. In an institution where it is called for only once in several weeks or months, at the crucial moment the gas cylinder is apt to be found empty or the knife dull, or some other circumstance occurs to interfere with successful manipulation. As it is always most easy to do that which one does every day, in our laboratories paraffin sections, for which everything is ready and the technician is in good practice, are apt to be good and frozen sections poor.

Frozen sections are apt to be thick, fragmentary and poorly stained. But, worst of all, frozen sections are most frequently asked for in cases of doubtful "lumps" in the breast. As uncertainty

whether such a lesion is "chronic cystic mastitis" or carcinoma not infrequently remains in the mind of the pathologist after the leisurely and thorough study of a number of large and well-made paraffin sections, what perplexity may result from the hasty examination of a frozen section, I leave to your imagination.

All that has been said thus far has to do solely with the preparation for the final step, which is the actual making of the diagnosis. This should never be entrusted to a technician. It can only be well done by a competent histo-pathologist, upon whose information, wisdom and experience it must rest. To one of such exceptional skill that he is able to make the diagnosis of cancer the moment a single cell is in the focus of his oil immersion lens, it may be small matter whether the section be good or bad. There are, however, very few that possess such power of divination, the majority of histo-pathologists fearing the consequences of errors that might follow such limitation of observation. The question is: "Is this a malignant tumor or not?"; and few seekers after the truth are willing to commit themselves until the means of arriving at it have been exhausted.

Finally, it is not always possible to arrive at a diagnosis. No pathologist is infallible and any one may err in judgment. There still remain tissues whose nature and disposition are uncertain, and some that are unknown. How fortunate for the pathologist is it that a diagnosis is, after all, not a fact, but only a well-founded opinion.

Prolegomena to the Life and Works of Ugo Benzi (1376–1439)*

By Dean P. Lockwood, Ph.D.

Professor of Latin and Librarian, Haverford College

Several years ago a fellow-student of Italian humanism called my attention to a group of manuscripts in the Library of Ferrara unknown to the learned world—unknown (and this is a very important consideration) because no catalog or inventory of these manuscripts had ever been printed and published. My friend, having been to Ferrara and seen for himself, told me that in this unknown collection he had run across a manuscript containing a better copy of Bruni's translation of the *Plutus* of Aristophanes than any I knew of, for I had recently published the text of this translation from a Paris manuscript. (If, at this point, I hear murmurs of *οὐδὲν πρὸς Ἀσκληπιόν* —or "what has this to do with the history of medicine?"—let me remind you that the *Plutus* of Aristophanes is a medical classic; you will find it in the *Bibliotheca Osleriana*.) Immediately (and this is another very important consideration) I ordered photographs of the Ferrara translation and found this version so great an improvement over the Paris copy that I decided at once to re-edit the work.

Well and good! When I had completed my studies, one important problem remained unsolved: what was the date of this version? Hoping to get some light from the *other* works in this manuscript (for, like many manuscripts of the XV century, it was a miscellany, i.e., the copyist took a blank-book and filled it up with as many works as it would hold)—I ordered photographs of the remaining pages. I now had the whole manuscript before me and had saved myself a trip to Ferrara!

I found that I had a veritable goldmine. Briefly the facts were these: about 1442 Giovanni Tortelli (destined later to become famous as librarian of the Vatican under Nicholas V, greatest patron of learning among the popes of the XV century) while resident in Bologna assembled a small group of literary and scholarly works reminiscent of one of the greatest intellectual events of the Italian Renaissance—the Ecumenical Council or World Congress of the Christian Church at Ferrara in 1438, summoned for the purpose of eliminating the doctrinal differences between the Greek and Roman orthodox Churches and effecting a union of the two halves of disrupted Christendom. Aside from being the most promising Church Congress ever planned (the promises, alas, came to naught), this was beyond doubt the most momentous meeting of scholars ever held in Europe, for it brought together the keenest minds of the new Italy and of the venerable Byzantine Empire, the direct heir of ancient Greek culture.

What then were the *Memorabilia* of the Council of Ferrara which Tortelli got together to be copied in his manuscript? They were: (1) the *Life of Ugo*

* Read before The College of Physicians of Philadelphia, the Section on Medical History, May 13, 1940.

Benzi, philosopher and physician, composed by his son, Socino; (2) the humanistic Latin translation of Plutarch's *Life of Romulus* made by Tortelli himself in 1438 while attending the Council in a humble capacity; (3) Bruni's humanistic Latin translation of the *Plutus* of Aristophanes, in a form probably produced in the company of Tortelli at Florence when the Council was transferred thither in 1439; (4) random notes by Tortelli on doctrinal problems discussed at the Council; (5) an *Outline*, in Greek, of arguments supporting the position of the Roman Church on the disputed question of additions to the creed—which *Outline* I believe to have been the work of the great Greek humanist, Bessarion (later Cardinal of the Roman Church and very nearly elected Pope). Thus Tortelli's little collection of *Memorabilia* constitutes a cross-section of the intellectual interests, both official and unofficial, of the Council of Ferrara, to wit, scholastic philosophy, humanism, and theology; or —to use modern terms, roughly equivalent—science, literature, and theology. Lest this seem fantastic, I hasten to add that the erudite Tortelli was but one of many men present at that Council who were capable of participating in the discussion of problems in science, literature, and theology—and to complete the picture of that spacious age, not yet narrowed by specialization, we might add to the above-mentioned departments of learning that of law.

Why should Tortelli have given first place in his *Memorabilia* to the *Life* of the physician, Ugo Benzi? To answer this question, let us picture to ourselves the amazing events of 1438 in the peaceful little neutral province of Ferrara, situated at the cross-roads between Lombardy, Venice, and the papal city of Bologna. In the early months of the year the delegates to the Ecumenical Council were assembling—they must have swamped the little town: first, Pope Eugene IV with many of his Cardinals and all his Court and many of the most celebrated scholars of Italy; second, the Byzantine Emperor of Constantinople (it was fifteen years before the capture of the city by the Turks) with his *eight hundred* horsemen and his Court; third, the Patriarch of Constantinople (who might be called the Pope of the Eastern Church) and other Levantine Patriarchs and churchmen; and finally, after an overland trip of several months by way of the Baltic provinces and Germany, came Isidore of Kiev, metropolitan of Russia, with his 200 followers (many of whom were destined, before the year was out, to succumb to the plague in overcrowded Ferrara). The host who had 'invited' all these notables to his capital was Niccolo d'Este, Marquis of Ferrara: astute, fat, and lustful; patron of learning and the arts, who was now in his 55th year and beginning to worry about his health. His court physician for six or seven years had been Ugo Benzi, now at the peak of his fame as the greatest physician in Italy.

And what connection did the court physician have with the Council? *Not*, I assure you, that which the local Board of Health would have with a 'convention' today! He did not take hygienic measures against the plague nor (so far as I know) attend the Russians or others who fell ill and died of it. It is characteristic of the age that he occupied the limelight, not as a *physician* (in our sense of the word), but as a scholastic philosopher. Playing the grand seigneur (since his grateful patient, Niccolo d'Este, had enriched him with estates and other bounties), he invited the learned men—Italians, Greeks, and Orientals alike—

to a brilliant banquet, after which *he*, the great Ugo, gave his guests an exhibition of his knowledge, for he discoursed "on the causes and origins of things, on the motion of the heavens, on the externality of the universe, on the immortality of souls, on the intelligences and God."[1] So famous did this occasion become that it was preserved in oral legend, and twenty years later the great humanist, Aeneas Sylvius (who subsequently became Pope Pius II), dressed the story up[2] to suit his own prejudices, making it more vivid perhaps, but certainly exaggerating Ugo's prowess, especially when he represented him as proposing for discussion "all (?) the topics on which Plato and Aristotle disagree; whereupon, giving his opponents their choice of sides, he refuted and silenced them one by one—thus Italy triumphed over Greece!"

One might infer from this account, as some modern scholars unfamiliar with the facts of Ugo's life have done, that Ugo was not only a philosopher, but a greater Greek scholar than the Byzantine Greeks themselves. That, of course, is nonsense: Ugo knew no Greek, but he was a great enough man in other ways to deserve our attention. He was the greatest professor and practitioner of medicine in Italy in the fourth decade of the XV century and he was the champion of Italy in that curious but all-important art of scholastic disputation. Let it not be thought, however, that he was a physician whose *avocation* was scholastic philosophy. It was the other way around: like all physicians of the middle ages he was a 'natural philosopher' whose interests were chiefly medical. A 'natural philosopher' might devote his spare time, as it were, to the practise of medicine. Relatively speaking, not enough was then known about pure medicine to occupy one intelligent person's *entire* energy and attention.

To return to our manuscript: like everything else in this small but valuable collection of memorabilia, the *Life of Ugo* has proved to be unpublished and unknown. As Barduzzi said in 1923, a study of Ugo Benzi's career was a great desideratum in the history of medicine, but Barduzzi had no inkling of the existence of this *Vita*.

Now Ugo was a *medieval* physician (the Renaissance of medicine did not begin for another hundred years), and his son Socino was a humanist.[3] This was a rare combination. Biography had been almost a lost art in the middle ages; the humanists had now revived it; but the humanists were not interested in contemporary scholastic philosophers and physicians—in fact, they had a very low opinion of their intellectual activities. Only filial piety, therefore, prompted the production of this unique humanistic biography of a scholastic medieval physician—and so unusual, so out of the ordinary run, was the product that it aroused no interest among contemporaries in either camp and was promptly forgotten. Tortelli's copy is probably the only one in existence.

But it is of even greater value than would at first appear, for we have no full-length biography of any medieval—nor, for that matter, of any ancient—physician. The *Life of Ugo*, therefore, is the earliest full-fledged biography of a physician that has been preserved to us—perhaps the earliest that ever was written, for even Hippocrates and Galen, great as they were, were not made the

[1] *Vita*, §26.

[2] *Europa*, chap. 52.

[3] He was also a physician, but that is another matter. Ugo was physician alone; Socino, physician *and* humanist.

subjects of *independent* biographies. Famous representatives of professions in the ancient world were treated by biographers only *en masse* and generally as a mere corollary to the history and evolution of the profession itself, cf. the *Lives of the Philosophers* by Diogenes Laertius, the *De viris illustribus* by Suetonius (who treats his subjects in professional classes—poets, orators, historians, grammarians, rhetoricians, etc.), the Preface on the history of medicine in Celsus *De medicina*, and the similar Preface on the history of law in the *Digest*. In medieval Italy, moreover, we have little more than verbal 'picture-galleries' of local celebrities, among whom physicians, such as Taddeo Alderotti of Florence, occasionally occur, but the sketches hardly ever get beyond a page in length and are quite anecdotal, relating a few scandalous details (like the size of Taddeo's fees) and telling apocryphal legends. But I have yet to find a complete and intelligent biography of any physician earlier than Socino's *Life of Ugo*.

And so, quite unexpectedly, I found myself studying the life and works of Ugo Benzi. Intending a chapter, I have written a book. Combining the facts related by Socino with available data from Italian archives, I have greatly enlarged the picture of Ugo's career and reinterpreted the life and thought of this typical representative of the medical profession in Italy in the first half of the XV century. I hope that I have fulfilled Barduzzi's expectations, for since Tiraboschi (the great XVIII century historian of Italian literature) wrote his brief and faulty sketch of Ugo's career, little or no attempt has been made to fill out the picture, in spite of the abundant archival materials that have been made available since Tiraboschi's day.

The first thing to note about Ugo's career is that it was inevitably academic. 'Medicine', being a subdivision of natural philosophy in his day, was primarily dialectical and theoretical. At the age of twenty Ugo received his first appointment, a lectureship on logic in the University of Pavia. Logic and dialectic were the foundation-stones of the medical edifice. A university career in the XV century, moreover, was generally peripatetic: Ugo, rising steadily in his profession and attaining (as was customary) to an important chair of medicine at about the age of thirty, reached the pinnacle of academic fame in 1430–31 at Padua; and having taught for thirty-five years, during which time he had held ten or eleven appointments (e.g., at Bologna during three separate periods), he retired from academic life at the age of fifty-five, to accept the lucrative and honorable post of physician to Niccolo d'Este, Marquis of Ferrara.

It is significant that he had taken up the *practice* of medicine only *after* he had attained distinction both as a professor or academic theorist and as a public disputant on scholastic 'science'. It was success as a platform debater on subtle Aristotelian problems of 'physics' (which included medicine) that brought rich and influential patients to a physician's door in the XV century. Ugo mounted the first rung of the ladder of fame in 1409–10, when, after serving his apprenticeship at Pavia, Bologna, and Siena and demonstrating his controversial powers at Perugia, he was appointed professor of medicine at Bologna (his second appointment in that university) and at the same time physician to Cardinal Balthasar Cossa, papal governor of the city. Before the academic year was over, Cardinal Cossa had become Pope John XXIII, at whose request Ugo is reputed to have defeated the haughty theologians of the

University of Paris in a public debate in Bologna. Thirteen years later Ugo was again professor at Bologna and physician to the then governor of the city, Cardinal Gabriele Condulmer, who in 1431, the year of Ugo's retirement from academic life, became the great Pope Eugene IV. Ugo was among those who welcomed this Pope to Ferrara in 1438 at the opening of the World Council. Of Ugo's famous banquet or symposium I have already spoken. A year and a half later Ugo died at the age of sixty-three.

But Ugo did not busy himself solely with the teaching and practice of medicine and with public battles and controversies in metaphysics and natural philosophy. He wrote and published many important works (to which I have given extensive study). They were, of course, the fruit of his professional activities.

(1) As a scholastic disputant he published a treatise on logic (now lost) and a number of *Questions*, i.e., actual lectures or arguments on such topics as humoral complexions, bodily growth, putrefaction, powers of the soul, etc. (some of these are preserved).

(2) As a professor of medicine he published his lectures, embodied in (a) his *Commentary on Aristotle's Parva naturalia* (now probably lost, though one or two 'questions' may be preserved from it) and (b) his vast *Commentaries* on the traditional Arabo-Latin texts of the ancient School of Salerno, to wit, the *Aphorisms* of Hippocrates, Galen's *Tegni*, and the three chief sections of Avicenna (I, 1–2; I, 4; and IV, 1). Remember that all these texts are in the venerable medieval Latin translations; Ugo and his ilk knew neither Greek nor Arabic. Ugo's *Commentaries* were for a hundred years among the standard textbooks of the Italian universities; long current in manuscript, they began to be printed in 1478; for almost fifty years (i.e., until 1524) they went through edition after edition; the most popular (the *Commentary on Avicenna I, 4*) was printed eleven times, the others five or six.

(3) As a medical practitioner he wrote over one hundred consilia, in which he recorded, after the fashion of his time, his treatment of individual cases. They were not definitively published, however, until after his death—perhaps not until long after. They too—between 1482 and 1523—went through five editions. Analogous to the consilia are his popular treatises in Italian on the Regimen of Health, chiefly the *Trattato circa la conservazione de la sanitade*. These treatises were not only printed in the XV and XVI centuries, but also in the XVII (1618 and 1620), almost a hundred years after Ugo's learned works had passed into oblivion.

No modern scholar has heretofore studied Ugo's works as a whole nor drawn any inferences from them concerning his life and thought. A slight beginning was made in 1921 by Castiglioni, who hastily published a few chapters of the *Trattato*[4]; and German historians of medicine, who belong to the "History of Science" school, have combed the Consilia and brought to light the few instances of Ugo's diagnosis and treatment that would bear modern inspection. But that attitude contributes little or nothing to the understanding of Ugo and his age. His works must be studied as a whole and must be seen in relation to their environment.

The presence on the shelves of the College of Physicians of copies of the *Trattato*, the *Consilia* (in the rarest and

[4] A further study by Garosi in 1933, concerning Ugo's relations to the governors of his native Siena, added very little.

most important edition), and the *Commentaries* on the *Aphorisms*, on Galen's *Tegni*, and on Avicenna I, *1–2* encouraged me to begin the study of the works.[5] Without the accompanying photographic copies, which I have been able freely to borrow, I should probably never have attempted to reconstruct the life and thought of Ugo.

It is very difficult to get any inspiration from the technicalities of Ugo's *Questions* and *Commentaries*. But the *practice* of medicine, throughout the ages, has a continuity which is based on the human factor. From the XIII to the XVII centuries, medical practice was mirrored to a remarkable extent in the *written* consilia. The habit of giving written advice and information to the patient or written suggestions (upon consultation) to the physicians who were treating the patient, though it had its drawbacks at the time, is a godsend to the historian who is trying to reconstruct the life of the period and the function of the physician in society at any particular time. The rich material of the medical consilia of the middle ages as a whole is awaiting the pen of a master historian.

I shall present in my finished work a preliminary outline of the range and character of all of Ugo's extant works and of his *Consilia* in particular. I shall leave it to others to carry on this work in greater detail and in special fields.

Above all, however, I must stress the need, in studying the works of Ugo or of any other medieval physician, of going *back* of the XV- and XVI-century editions, all of which, by modern standards, were poorly printed and were repeatedly revised *ad lib.* by editors who had no more respect for them than for any other textbooks—back to the manuscript books of Ugo's own day; to such texts as the great 1428 copy of the *Commentary on the Aphorisms* now in the Osler Library at McGill University. No one has ever instituted a world-wide search for early manuscript copies of the works of Ugo. They may turn up anywhere today from Toronto to Budapest, from Edinburgh to Naples. I have not had the opportunity to make such a search. I have profited much, however, from the generously published hints of Prof. Lynn Thorndike, whose studies of manuscript sources for XV-century 'science' have been epoch-making; and I have myself browsed in the Vatican, where, with the help of friends, I have uncovered many treasures (still uncataloged and unknown to the learned world).

The final chapter of my book will deal with Ugo's character and personality—a problem whose solution will throw light on the whole concept of medicine in the middle ages. To what qualities did Ugo owe his success as a physician? Obviously he was no scientist nor had he any of the qualities that go to make the true scientist of today. But he *did* have certain talents and certain traits that accounted for his success in his chosen career. They were: (1) unconquerable ambition and tireless energy—such traits, of course, are universal and cast no particular light on the middle ages; (2) an outgoing, optimistic, cheerful personality—which no doubt made him popular in the classroom and at the courts of princes and lent charm to his bedside manner; (3) a remarkable memory, photographic in its ability to hold words and facts: consequently he was a walking encyclopedia of sheer knowledge, a pugnacious pedant, proud of the extent of his information and never tired of "talking shop"; (4) a quick wit

[5] Only two commentaries are lacking in Philadelphia; they are available in the Army Medical Library at Washington, and elsewhere.

and a sharp tongue, keenness in oral debate, self-confidence and arrogance in challenging others to the test of disputation and controversy. Ugo showed these qualities at an early age.

Ugo, in short, was a scholar (according to the accepted standards and obligations of scholarship in his day) and a great one. But, difficult as it may be for us to reconcile Galenic theory with successful practice, he was also a great healer. He healed rich and poor, and Socino claims that his advice was sought on practical problems by physicians "not only of Italy, but also of Germany, Spain, Britain, and other foreign lands."[6] The truth of this assertion is borne out by the great consilium no. 38, in which Ugo, consulted by letter from Spain, discusses symptoms, diagnosis, and prognosis of a severe case of asthma and writes two complete dietary and medicinal regimens, one for use during attacks of the disease, the other for the guidance of the patient during periods of normal health.

Finally, we need not doubt the sincerity of Tortelli's own statement, repeated by Symphorien Champier and others, that the honor of being *Prince of Physicians* passed from Giacopo della Torre of Forlì (who died in 1413) to Ugo Benzi of Siena. It is no exaggeration to say that for the last twenty years of his life Ugo was at the head of his profession in the European world. It was not a period of progress in medicine, but for that reason it is all the more typical of the scientific thought of the middle ages. Given the unique and extensive materials that are now available, I trust that my study of Ugo's Life and Works may contribute something to our knowledge of medieval medicine in its relationship to the society which supported it.

[6] *Vita*, §22.

Memoir of David Ralph Bowen, M.D.*

By Ralph S. Bromer, M.D.

Doctor David Ralph Bowen, a Fellow of this College since 1919, died in the Pennsylvania Hospital, September 6, 1939, after an incapacitating illness which dated from 1931. During that period he lived the life of a semi-invalid, and among his possessions at the time of his death were autobiographical notes which he had written at sundry times during the eight years of his physical disability. These have been kindly loaned to me by his family in the preparation of this memoir.

Dr. Bowen was born on Southwick Farm near Owego, New York, June 3, 1872. He was of the tenth recorded generation of the Bowen name, the first known ancestor being Richard Bowen, born in Wales in 1585. His father was Cyrus Fuller Bowen. His mother, Hannah Maria Brown, was of the twelfth generation descended from John Alden and Priscilla Mullens. From his father he inherited what he termed in his notes his "inventive tendency," which later in life expressed itself in the planning and production of numerous improvements in roentgenological technique.

His boyhood was spent on the farm, where his activities were somewhat restricted by poor health and a small stature. At the age of fourteen he entered Wyoming Seminary, a Methodist School near Wilkes-Barre, Pennsylvania. Of this school with its strong religious emphasis, he wrote, "I owe much to its formation of my character." He graduated in 1891 and entered Jefferson Medical College the same year. He completed his medical course in 1894, having just passed his twenty-second birthday. Because of his youthful appearance he was unable to secure an internship and he began practice immediately in Orleans, New York. Between 1895 and 1906 he moved six times, although he was regarded as a successful country practitioner in each community. He attributed this to a strong wanderlust and an inferiority complex which at the time he did not recognize as such.

In 1906, while associated with two other physicians in Rome, New York, he found a discarded x-ray coil and interrupter which in other hands had been a total failure. After much experimentation and study, he achieved a working knowledge of the apparatus and, thus, he began his roentgenological career. The roentgenograms he secured could not be compared with those obtained with the roentgen apparatus of the present day, but the results were considered satisfactory and were regarded by his colleagues in the clinic as a distinct advance in diagnostic methods. In 1907 he studied for two weeks with Dr. Sidney Lange in Cincinnati, Ohio, and while there he attended the meeting of the American Roentgen Ray Society. At this meeting he acquired "an exaggerated impression of the importance of extreme precautions" against roentgen-ray reactions. This always remained with him and he constantly impressed his students with the necessity of efficient protection. At the time of his death, he was entirely

* Read January 8, 1940.

free from any ill effects of roentgen irradiation.

During the years 1907 and 1910 he sought an opening in roentgenology in a larger city than Rome. At an informal meeting of roentgenologists in New York City in December, 1910, he met the late Dr. Willis F. Manges of this city, who was in need of an assistant, and in 1911 he began his association with Dr. Manges, both in private practice and in the Department of Radiology of Jefferson Hospital. In the same year he was appointed radiologist to the Pennsylvania Hospital on a part-time basis. During the war years, 1917–1918, he carried on the work of Dr. Manges in their office and in the Jefferson Hospital. In 1920 he severed his connection with Dr. Manges and the Jefferson Hospital and devoted his entire time to the Department of Radiology of the Pennsylvania Hospital. With exceptional ability he soon developed an efficient organization and brought the department to a high standard before he suffered his first serious illness in 1931.

When he attended the meeting of the American Roentgen Ray Society in 1907 he was impressed with the benefit gained by association with other physicians of his speciality. When elected a member he became an ardent and enthusiastic participant in its activities. He attended every annual meeting from 1907 to 1931 and was elected President of the Society in 1919. He was always much interested in the Philadelphia Roentgen Ray Society. The Midwinter Conference of Eastern Radiologists, organized in 1926, has recently been described as a monument to his untiring efforts.

Throughout his entire service at the Pennsylvania Hospital he trained students in radiology. In his teaching he continually emphasized precise technical procedures, the maintenance of a strict ethical code and the sympathetic management of patients and their families. His influence on the practice of radiology was felt especially in Philadelphia. Dr. Manges wrote to him after his first illness, "I am sure that the ethical status of roentgenology in Philadelphia is better than in most cities, and that much of it is due to your personal character and influence."

Dr. Bowen made many contributions to roentgenological literature. A great proportion of these were descriptions of new devices and original technical methods, contributed when roentgenology was still in its infancy, such as a knee rest to be used in examination of the spine and kidneys, a posturing instrument for examination of the feet and lower extremities, a device for accurately centering an x-ray tube in the tube stand, and many others. His first "invention," in 1911, was a plate rocker to accommodate four trays, one above the other, operated by a reciprocating motor which he secured from a manufacturer of washing machine motors. He was among the first to design and advocate the use of tank development of x-ray films. In 1924, when a Department of Technique was established in the *American Journal of Roentgenology and Radium Therapy*, he was appointed its first editor.

In 1895 he was married to Mary A. Moe. Five children were born to them. Mrs. Bowen died of influenza during the epidemic of 1918. In 1919 he married Edith Warrington, who with the five children survives him.

Dr. Bowen's interest in the development of roentgenological technique did much to prevent the new speciality from becoming mere laboratory routine performed by lay technicians. He demon-

strated that physicians as well as electrical engineers were needed to develop roentgen apparatus and methods of examination of patients. He always considered himself a roentgenological clinician and consultant and never hesitated to defend this ideal with vigor. Roentgenology through his death has lost one of its pioneers, not one to be considered among the early martyrs to the new discovery of Roentgen, but one whose guiding hands, during its early growth, aided in placing it on a firm and lasting foundation.

Memoir of Frederick J. Kalteyer, M.D.*

By Randle C. Rosenberger, M.D.

DR. FREDERICK J. KALTEYER, who for more than forty years practiced medicine in Philadelphia and vicinity, died December 21, 1938, at his residence, 1707 Spruce Street.

He was born in San Antonio, Texas, July 21, 1873, his parents being George H. and Johanna Kalteyer. He was an only son and his father, having built the first cement factory in Texas, wanted Fred to study engineering and architecture, but having come from a family of chemists and physicians, he decided to study medicine.

He attended the public schools in San Antonio, at fourteen a preparatory school in Philadelphia, and later the medical school of the University of Pennsylvania. He was graduated from the University of Pennsylvania in 1895 and was also graduated from the Jefferson Medical College in 1899.

Following his graduation from the University of Pennsylvania he spent six months in Johns Hopkins Hospital and then served an internship in the German Hospital, now the Lankenau. During this service he came under the notice of Dr. J. C. Wilson, one of the attending physicians and the Professor of Medicine at Jefferson Medical College. Following his internship he came to Jefferson, interested himself in medicine and pathology and for a time taught hematology in this latter institution.

Then came a service which lasted for almost forty years, of a devotion to internal medicine; he taught the principles of medicine and physical diagnosis up until the time he was incapacitated by illness. He was principally interested in internal medicine and became Clinical Professor of Medicine under J. C. Wilson and Thomas McCrae.

He was a keen observer and a rather strict disciplinarian, thoroughly loving his work and insisting that his lectures begin promptly at the stated time and generally last the full sixty minutes. While a member of the teaching staff at Jefferson in his early years he served as Assistant Pathologist to the Philadelphia General Hospital.

On account of his devotion to his work his services were solicited by other hospitals than Jefferson and he became physician to St. Joseph's, Philadelphia General, Pottstown, the Delaware County Hospital, Frankford and St. Mary's. He took a great interest in the Interstate Post Graduate Assembly of North America and was elected an Honorary Member of this body and served as assembly chairman by appointment in 1934. He was a member in good standing of the American Medical Association, the State and Philadelphia County Medical Societies, the College of Physicians of Philadelphia, to which he was elected in 1903, American College of Physicians, American Therapeutic Association, Pathological Society, Meigs Medical Association and the Medical Club of Philadelphia. He was a member of the Alpha Tau Omega, Alpha Kappa Kappa, of the Old Merion Cricket Club and of the University Club and served on the Board of Governors of the latter.

* Read January 8, 1940.

He was also a member of the Naval Reserve and held the rank of Lieutenant-Commander.

He was very fond of taking long walks and at various times recommended this form of exercise to the students he taught. With all his hospital connections and teaching assignments, he was able to contribute a volume on "Modern Medicine," with Julius Salinger as co-author, in 1900, and also revised "The Complete Medical Pocket-Formulary" by J. C. Wilson, in 1907. While in the Department of Pathology and teaching hematology he also published privately "Laboratory Demonstrations on Hematology."

Jefferson Medical College has lost a devoted, thorough and conscientious teacher; in the words of a sister still living, "he was a great student and lived for his profession." Not only did the institution where he taught so long and faithfully lose a valued friend but the medical profession lost a most valued member. In 1938 Dr. Kalteyer was married to Miss Marie Camblos, who survives.

Memoir of Floyd Elwood Keene, M.D.*

By George P. Muller, M.D.

FLOYD ELWOOD KEENE, a Fellow of the College, died November 15th, 1938. His passing was a moment of great sorrow to his friends and colleagues and a distinct loss to the medical profession of this city.

Dr. Keene was born at Kewanee, Illinois, October 6th, 1881, a son of John E. and Lalla Rooke (Robinson) Keene. His father during his early life was a Methodist minister. He was educated at Peoria, Ill., to which place the family had moved in 1886, and, deciding to study medicine, was graduated from the University of Pennsylvania in 1904. He was one of the outstanding and scholastically brilliant members of his class and thus was selected as an interne in the University Hospital. I first came into contact with Keene then and can well recall the intelligent coöperation which he gave to all of his chiefs. This, together with his own charming personality must have made an impression upon Dr. John G. Clark, as manifested by subsequent events.

At the conclusion of his interneship he went to Berlin and Vienna for postgraduate study during 1907–1908. His particular object was to obtain training in the use of the cystoscope especially in women, and in diseases of the urinary tract.

When he returned to Philadelphia he immediately attached himself to the Gynecological Service of Dr. John G. Clark where his knowledge of cystoscopy in women led to the formation of what virtually was a department of cystoscopy. He worked in the out-patient department and became an Instructor in Gynecology. In a short time a vacancy occurred by reason of the departure of Dr. John Luther and now Keene's hard work and wonderful personality bore fruit and Dr. Clark asked him to be his private assistant. I have seen many people operated on by Dr. Clark and always they recalled Keene with respect and affection. He was an ideal assistant. He was elected a Fellow of this College in 1912.

His efficient work as a teacher and as a gynecologist soon led to promotion and in 1922 he became Assistant Professor of Gynecology in the Medical School of the University of Pennsylvania.

During these earlier years Keene wrote a dozen papers on miscellaneous subjects mostly of an urological nature but in 1921 in association with Clark he published the first of numerous papers on cancer of the uterus and especially its treatment by radium. In 1922, again with Clark, he wrote the first of a series of papers on benign or functional uterine hemorrhage and still later, in 1927, he began to write upon endometriosis. These three subjects were uppermost in his mind and the most important of his literary output and he became an authority on the use of radium in the treatment of both benign and malignant uterine lesions.

It is curious that he never wrote upon the technical aspects of his specialty because he soon became an exceedingly skillful operating gynecologist. His re-

* Read February 7, 1940.

pair work on the perineum was beautifully done and his abdominal hysterectomy a thorough, careful, workmanlike job. Earlier he did various operations in the abdomen but later confined himself entirely to the female organs and the urological tract.

Floyd Keene was fortunate in his nearly twenty years' association with John G. Clark, unmarked by anything but mutual admiration and assistance to each other. He learned to operate, to investigate and to teach and became one of the best clinical teachers in the Medical School. When Clark died in 1927, there was no question but that Keene would succeed and he was elected William Goodell Professor of Gynecology in 1927.

He organized his department and almost overnight, became the leading gynecologist in Philadelphia partly because of the aegis of the University, but mostly because of that engaging personality that had served to carry him up to the seats of the mighty.

After 1927 he published twenty-one papers usually associated with one of his assistants, especially Robert G. Kimbrough or Franklin Payne. He continued the high order of his teaching and his operative technic and also developed the largest and most lucrative gynecological practice in Philadelphia. Through it all Floyd Keene remained the same genial, coöperative, friendly man that always he had been. Success did not spoil him and he never became dictatorial or egotistical.

Keene always remained a practicing gynecologist and a teacher of gynecology. His special activities were in the American Gynecological Society, the Gynecological Club and the Obstetrical Society of Philadelphia, in all of which he was in the forefront of leadership and was variously elected President of all three.

In 1916 he was Chairman of the Surgical Section of the Pennsylvania State Medical Society. He was a Fellow of the College of Physicians of Philadelphia and the Philadelphia Academy of Surgery, and the American College of Surgeons. He was on the Editorial Board of *Surgery, Gynecology and Obstetrics* and I well recollect the high esteem with which he was held by the late Allen Kanavel, the Editor of this Journal. He was of the Phi Delta Theta, Alpha Omega Alpha and Phi Alpha Sigma fraternities.

He was consulting gynecologist to the Chestnut Hill, Bryn Mawr and Abington Memorial Hospitals.

If we go back a few years to the war period we find that Keene together with many of the University Hospital group, became a member of Base Hospital #20. Early he was sent to Washington and nearly was sent for duty with the British Army. Subsequently he was sent for training in the course on brain and nerve surgery at the College of Physicians in New York. However, he was pulled back to Base Hospital #20 and signed the Red Cross Muster Roll on May 23rd, 1917. They sailed for France on April 22nd, 1918, and arrived at Chatel Guyon on May 7th, 1918. On July 21st he left Chatel Guyon for the front with team #61 and saw service on practically all of the American battlefronts. At the close of the war and after the discharge of all patients from the hospital he sailed for home from Brest on April 6th, 1919, and was discharged with the rank of Major, M. C., during the week of April 21st, 1919.

After the Armistice, Floyd Keene had time for other things than war and he

met and wed on January 27th, 1919, Mlle. Marthé Bussiére of Chatel Guyon. Throughout the ensuing nineteen years their married life was ideal and two children were born, Jeanette and John Clark Keene.

My own acquaintance with Floyd Keene dated back to his interne days in 1904, one year after I became an Instructor in Surgery. In later years we became close friends, spent most of our vacation periods together, and played golf together nearly every week-end at the Country Club. During that time I never heard or knew him to speak ill of any colleague. He might be critical at times of the medical opinions of others but as he would say, it was all in the game. I never knew a man in so high a position who was so generally liked. His life and achievements should serve as a model to the younger generation.

Memoir of George Melick Boyd, M.D.*

By Lewis C. Scheffey, M.D.

THE desirable quality of modesty is not always a characteristic of those who attain distinction, but this fortunate synthesis was exemplified in the person of George Melick Boyd, whose memory it is our privilege to honor. Gentleness and courtesy, too, combined with ability, courage and Christian virtue to round out the career of one respected and beloved by all who enjoyed his acquaintance and treasured his friendship.

From early boyhood, George Boyd found much happiness in the world of nature. Roaming through the woods and about the countryside, he soon developed that artistic sense, destined, in later years, to become articulate in brush and color. Likewise came a zest for fishing, an avocation which he followed steadfastly throughout those recreative periods that interrupted a busy professional routine. When, in the sunset of life, George Boyd answered the final call, it seems ever so fitting that it should have been at the close of a happy day on the trout stream, in the companionship of his cherished family.

Dr. Boyd was of distinguished lineage. He was born in Philadelphia on August 11, 1861, at the time when George Brinton McClellan, acclaimed by the North as the man of the hour, was speculating about dictatorship in his Washington headquarters, following McDowell's disastrous defeat at Bull Run a few weeks before. The Boyds were of Scotch descent. George Boyd, his father, was a well-known wholesale grocer of Philadelphia. His paternal grandfather, the Rev. Dr. George Boyd, son of Robert Boyd, a Revolutionary soldier, came from New York State, and was the first rector of old St. John's Protestant Episcopal Church, situated on Brown Street east of Third in the district of the Northern Liberties. The cornerstone of this historic edifice, the fifth church to be established in old Philadelphia, was laid in 1772, the church being consecrated by Bishop White in 1816. The first Protestant Sunday School in the city was organized here by the Reverend Mr. Boyd in an old wooden building in which the first church services were conducted. In 1839, in recognition of his conspicuous career, The University of Pennsylvania bestowed upon him the honorary degree of Doctor of Divinity. A daughter, Catherine, became the first wife of Charles Nicolaus Buck, a German who emigrated to Philadelphia, where he became an importer and served from 1817 to 1844 as Consul General of the Free Imperial City of Hamburg.

The other great grandfathers of Dr. Boyd likewise took part in the Revolutionary War. One was Peter Melick, a Pennsylvanian, who served with the Continentals at Valley Forge, and later fought the Indians at his frontier home in the neighborhood of Bloomsburg. He and his family barely reached the safety of Fort Wheeler when a marauding band attacked and burned their house. The other, Robert H. Livingston, of New York, was a descendant of that Robert Livingston, also of Scotch ancestry, who

* Read March 6, 1940.

became first Lord of the Manor in New York State, and was the direct ancestor of famed Chancellor Livingston.

The renowned Joseph Leidy was a cousin of Dr. Boyd, and his preceptor. It may be recalled that at the first lecture of the Joseph Leidy Memorial Foundation on April 17, 1913 (given by Prof. Edmund Beecher Wilson, of Columbia University), Prof. Charles S. Minot, of Harvard, in paying tribute to the memory of Dr. Leidy remarked: "Extreme modesty was a marked characteristic of Joseph Leidy's throughout his life, and was accompanied by an animated unselfishness which endeared him alike to his friends and students." That similar traits, therefore, were revealed in the character of his kinsman is not surprising; neither is it strange that the attributes of the naturalist and artist, exhibited in so great a degree by Dr. Leidy, found expression in Dr. Boyd's life.

He attended school at the Rittenhouse Academy and at Dr. Ferris' Classical Academy in Philadelphia, entering the Medical School of the University of Pennsylvania in 1879, and graduating with honorable mention in the Class of 1882. Among his classmates were Howard A. Kelly, Judson Daland, Charles P. Henry, William J. Taylor, McCluny Radcliffe and Howard Fussell.

A paragraph of a contemporary newspaper account of the graduation exercises held at the Academy of Music that year was headed "NO FLOWERS" and went on to state: "The usual sight was not witnessed of a procession of fresh young M.Ds., apparently going into the horticultural business, struggling homeward with their hands filled with bouquets and baskets of flowers hanging on their arms. All presents were sent to the back door where the graduates got them when the exercises were over. They were mostly in bundles and consisted of books, instruments and other articles which the young men will find useful in their profession."

Following graduation, Dr. Boyd served a two-year internship at the Episcopal Hospital, continuing there as Assistant Surgeon until 1894, when he resigned to devote his time entirely to obstetrics and gynecology. During this period, transportation to that part of the town was by means of "dummy engines," a sort of trolley car with a steam engine trailer. They went as far as Frankford. Passengers tried to keep their feet warm in the straw on the floor of the car in winter, and climbed to the roof to keep cool in summer. Round rubber buttons, with a hole in the center, were sold by the conductor, six for a quarter, and these served as fare tokens. As the trolley line was somewhat removed from the hospital, it was necessary to walk the intervening distance in all kinds of weather.

In 1888, Dr. Boyd was appointed Assistant Surgeon to the Kensington Hospital for Women. During the same year he assisted Dr. Howard A. Kelly, founder of the institution, with the first cesarean section, successful for mother and child, that had been accomplished in Philadelphia in over fifty years; for it was in 1835, and again in 1837, that Professor William Gibson had without fatality performed the operation upon the same patient, securing a live infant on each occasion. It was quite a coincidence, therefore, that in 1890 Dr. Boyd should assist Dr. Charles P. Noble with a second successful cesarean upon Dr. Kelly's patient of two years before.

Dr. Boyd became Visiting Physician to the Philadelphia Lying-In Charity Hospital in 1890, soon after the new

building had been provided at Eleventh and Cherry Streets. Associated with him on the staff were his good friends Drs. Oliver Hopkinson and W. Reynolds Wilson. He continued active work there until 1923, when he became Consulting Obstetrician, retiring from this position in 1930. He was also Consulting Obstetrician to the Philadelphia General Hospital and to the Preston Retreat over a period of many years, positions which he held until his demise.

Dr. Boyd's active teaching career covered many years. Appointed Demonstrator of Obstetrics in the Medico-Chirurgical College in 1895, he became successively in the same institution Clinical Professor of Obstetrics in 1898, Professor of Clinical Obstetrics in 1901, and finally Professor of Obstetrics in 1910, his predecessor being Prof. Haehnlen. When the College merged with the University of Pennsylvania in 1916, he was appointed Professor of Obstetrics in the Graduate School, a chair occupied until 1935, when he became Emeritus Professor. During this latter time Dr. Boyd was Obstetrician and Gynecologist to the Graduate Hospital. As a teacher he was earnest, practical and well-liked by his pupils. He used many original drawings and lantern slides to illustrate and emphasize particular points to his audience. Sensitive in nature, his address, while not vehement, was sincere and meticulous; he was always the gentleman in his contact with students and associates. Many will recall the hospitable evenings spent at his Spruce Street residence when he entertained the members of the student obstetrical society named in his honor. No one has expressed to me more admiration of Dr. Boyd, than has his assistant and associate of thirty years, Dr. Charles B. Reynolds.

Fellowship with the Obstetrical Society of Philadelphia was long and active. After his election to membership on October 4, 1888, there was seldom a meeting during the ensuing fifty years which he did not attend. He contributed freely to the programs, both in discussion and with presentations. The majority of his papers dealt with obstetrical subjects. He was especially interested in cesarean section, writing from his own pioneering experience with the operation in the early days of aseptic surgery. At one of his first cesarean clinics, 500 spectators were reported to have been present in the old Medico-Chi amphitheatre. With this procedure he was eminently successful, reporting 48 cases from 1896 to 1914, without the death of a mother and with the loss of but two babies. From that time on, only two patients succumbed to this operation, one in 1916 and one in 1919. These were his only cesarean deaths, which, in an operating experience of forty-odd years, is an enviable record. One of his successful cases is especially noteworthy. The patient was a midget, one Martha Ramsey, known as the "Queen of the Lilliputians," and a vaudeville performer. She was 3 feet, 10 inches tall and weighed 57 pounds (a brother incidentally was nearly 7 feet tall, while two others were midgets). Her infant weighed 4 pounds, and the operation was resorted to because of a dwarfed pelvis with a conjugata vera of 5 cm.

Dr. Boyd was chosen President of the Obstetrical Society in 1912, and was re-elected in 1913. In December of the latter year he suffered a serious illness as the result of an infection incurred while operating. This prevented him from being present at the dinner and reception which he gave at his home in honor of Dr. Reuben Peterson, then

Professor of Obstetrics and Gynecology at the University of Michigan, whom he had invited to address the Society as guest speaker at that time. The last paper presented before the Obstetrical Society by Dr. Boyd was in 1930, and was entitled "Extrauterine pregnancy at full term—a report of two cases with original illustrations." Continuing to maintain his interest in society affairs, he was made an honorary member on March 3, 1938.

Dr. Boyd likewise appeared on the programs of the American Medical Association and of various state societies. He was particularly active in the meetings of the Section on Gynecology of the College of Physicians, which was in existence many years ago. He was primarily an obstetrician, and an excellent one. He was left-handed; his hands were small and well adapted to obstetric manipulations. Gentle, self-controlled, and never hasty, his was the gift of equanimity. These qualities, combined with adequate experience, made him a skillful diagnostician. He was an able gynecologist as well.

Dr. Boyd became a Fellow of the College in 1891. He was a charter member of the American College of Surgeons, and early in his career joined the American Medical Association and his State and County Societies. He was also an honorary member of the Delaware State Medical Society. An unusual honor was accorded him in 1936 when he was elected President of the Philadelphia Alumni Association of the Medical Department of the University of Pennsylvania. The Phi Kappa Sigma Fraternity claimed his allegiance and he held membership in the Cincinnati Society of New York, and in the Historical Society of Pennsylvania.

During World War I, Dr. Boyd served as Captain in the U. S. Medical Reserve Corps, and was Surgical Chief at Camp Sevier, N. C., where thirty-seven medical officers comprised his staff.

On Nov. 12, 1890, in Grace Episcopal Church, then on Twelfth Street above Arch, Anna Gillespie became his bride. Mrs. Boyd was the daughter of Thomas L. and Mary C. Gillespie, of Philadelphia. Mr. Gillespie was a well-known merchant, financier, philanthropist, and humanitarian, associated with a group of charitable institutions and organizations. Among these was the Philadelphia Lying-In Charity Hospital of which he was onetime president. Dr. Boyd's home life was tranquil and happy; he enjoyed the companionship of his children and entered eagerly into their activities. Mrs. Boyd, the gracious lady who survives him, was vitally interested in his work. She was in every sense a loving companion, and to her he was devoted. The son and daughters are: George Boyd III, Mrs. Murray Spahr, Jr., and Mrs. Galloway C. Morris III.

He loved to travel, to paint and sketch in the outdoors, and several times his work received honorable mention in the art exhibitions of the Seymour Haden Society of the University of Pennsylvania, notably a water sketch of Green Point, Nova Scotia, and one of canoeists paddling over a pine-bordered northern lake at dawn. Snow scenes in the Poconos were favorite subjects with him.

Usually Dr. Boyd and his family spent a part of the summer months in camps—for many years at Belgrade Lakes in Maine, and more recently in Nova Scotia, in the vicinity of beautiful and historic Annapolis Royal. During these summer holidays bass and trout fishing were his special enjoyments. In May of 1939, the Boyds decided to accompany their son-in-law and daughter (Mr. and

Mrs. Spahr) on a trip to the Beaverkill Stream in Ulster County, New York. Dr. Boyd was enthusiastic about the spot selected; he had thoroughly enjoyed a day of fishing, when on the evening of May 20, 1939, a heart ailment, sudden in onset, proved fatal.

George Boyd was a devout churchman, and a member of St. James's P. E. Church. His life embodied his religion; he exemplified the golden rule. Although honored and given precedence over many of his fellows, he was ever unobtrusive and inclined to disparage his achievements. To my mind, he typified the humble thought expressed in the prayer uttered by the Breton sailor when putting out to sea,—and which he was wont to quote—: "Keep me, my God: Thy ocean is so great, and my boat is so small!"

Transactions of the Sections

SECTION ON GENERAL MEDICINE

Regular Meeting, March 25, 1940

The Clinical Use of Testosterone Propionate. James E. Cottrell, M.D. (*Abstract 1, below.*)

Leptospirosis Icterohaemorrhagica (Weil's Disease); Report of a Small Outbreak in Bathers near Philadelphia. W. Paul Havens*, M.D., and Carl Bucher, M.D. (*Abstract 2, below.*)

An Evaluation of the Electrocardiograph for the Practitioner. Josephus T. Ullom, M.D. (*Abstract 3, below.*)

Mitral Stenosis in Elderly Persons. Stanley E. Harris, M.D., and David Riesman,† M.D. (*Abstract 4, below.*)

Regular Meeting, April 22, 1940

Heparin in the Treatment of Subacute Bacterial Endocarditis, with a Report of Three Cases. Joseph C. Doane, M.D. (*Abstract 5, below.*)

Citrated Plasma in the Treatment of Secondary Shock. Max M. Strumia, M.D., Joseph A. Wagner*, M.D., and J. Frederick Monaghan*, M.D. (*Abstract 6, below.*)

Boeck's Sarcoid. David A. Cooper, M.D. (*Abstract 7, below.*)

Sarcoid Disease, with a Review of Modern Concepts of Tissue Immunity. Carmen C. Thomas*, M.D. (*Abstract 8, below.*)

* *By invitation.*

† Died June 3, 1940.

Regular Meeting, April 27, 1940

Rupture of the Pulmonary Artery in Fatal Hemoptysis in Pulmonary Tuberculosis. Robert Charr, M.D., and J. Woodrow Savacool*, M.D.

Total Myxoedema. George C. Griffith, M.D., and R. Philip Custer, M.D.

Hereditary Ectodermal Dysplasia. F. William Sunderman, M.D.

A Study of 230 Consecutive Cases of Diabetic Acidosis. Joseph T. Beardwood, jr., M.D., and George P. Rouse*, M.D.

Abstracts

1. The Clinical Use of Testosterone Propionate. James E. Cottrell, M.D.

Ten ambulatory male patients have been observed and treated with testosterone propionate, which is one form of androgenic sterol producing most of the biological effects of the male sex hormone. Beneficial effects were most marked in adult males with hypogonadism and fairly satisfactory in adolescent type of hypogonadism. Therapeutic results in the male climacteric and in male sterility were disappointing.

These experiences lead to the following suggestions: Testosterone propionate can be depended upon to relieve most of the symptoms of deficiency of male gonad hormone. Before resorting to the therapeutic use of androgen an attempt should ordinarily be made to stimulate the patient's own gonads with gonadotropic substances. As treatment with testosterone propionate is substitution ther-

* *By invitation.*

apy, the effect can be expected to regress when administration is stopped; but the effect may be maintained with much smaller doses than are required to produce the initial effect. Lack of sexual power is not of itself an indication for treatment with testosterone propionate—additional psychic or social indications are required. There is reason to suspect that when testosterone propionate is administered to a man who does not actually lack gonad hormone little or no effect is produced. Hence, testosterone propionate may serve as a therapeutic test for hypogonadism.

2. Leptospirosis Icterohaemorrhagica (Weil's Disease); Report of a Small Outbreak in Bathers near Philadelphia. W. Paul Havens, M.D., and Carl Bucher, M.D.

In 1914 Inada and Ido described a spiral form of microörganism as the etiological agent of Weil's disease. Although the first proved cases of this syndrome occurring in Great Britain and the United States were reported in the same year (1922), subsequent reports have listed 248 cases in the former and only 22 in this country. It is suggested that this discrepancy may be due to the facts that more interest is manifested abroad in this disease and that serodiagnostic and cultural methods, which are more commonly applied in Europe, are frequently necessary for diagnosis, since jaundice occurs in less than 50 per cent of cases.

In July 1939 seven young men, bathing in a stream possibly polluted by infected rats, contracted an acute infectious disease in varying grades of severity. Five were affected mildly and two were seriously ill with fever, jaundice and hematuria. One of the two severely ill patients died. Biologic studies of the fatal case and serologic evidence in the other severe case proved a diagnosis of leptospirosis icterohaemorrhagica. Clinical and epidemiologic evidence suggested a similar diagnosis in the mild cases, although serologic proof was lacking.

3. An Evaluation of the Electrocardiograph for the Practitioner. Josephus T. Ullom, M.D.

Before the introduction of the electrocardiograph, diagnosis in cardiac disease was based entirely upon the history and physical diagnosis. After the introduction of the electrocardiograph, painstaking, careful investigations by Mackenzie and Lewis and their co-workers, and a host of brilliant young men in this country, have elucidated the changes in rate and rhythm and there has arisen an orderly classification and nomenclature. The electrocardiograph has definitely clarified the situation with regard to these abnormalities.

Perhaps its greatest value to the practitioner has been in the diagnosis of coronary thrombosis. While this disease can usually be recognized clinically, the electrocardiogram provides a clear-cut and precise diagnosis which is demonstrable to the patient and which helps to emphasize the need for prolonged rest so important to the best results.

The electrocardiograph, while not an absolute essential to the practitioner, is of prime importance and assists materially in an exact and scientific diagnosis.

4. Mitral Stenosis in Elderly Persons. Stanley E. Harris, M.D., and David Riesman, M.D.

There is a type of mitral stenosis which appears past middle life and which is in no way related to rheumatic infection.

Five cases are presented in which in the dorsal decubitus a presystolic murmur heard over a small area near the apex developed during the period of observation. In these four women and one man, all over forty years of age when the murmur was first detected, there was no history suggestive of rheumatism and no aortic regurgitation or evidence of dilatation of the left ventricle. Only one of our cases has died and no autopsy was obtained. However, the pathologic findings in this condition have been described by Allbutt, Huchard, Newton Pitt, Goodhart, Boas and Perla and others. They are a funnel-shaped, or more often an irregular, narrowing of the mitral orifice due to atheromatous changes in the valve and particularly of the auriculoventricular ring.

From our cases it may be concluded that: 1. The condition is more common in women. 2. It begins in middle life or later and is slowly progressive. 3. To discover the murmur the patient must be examined both standing up and lying down. 4. For years it produces no symptoms. If the patients are short of breath it is more often from obesity than from cardiac dysfunction. Only two of our cases have become decompensated. 5. The prognosis is good. Death comes late. In our single fatal case death occurred following a series of embolic phenomena. 6. Disease of the gall bladder is a common accompaniment.

5. Heparin in the Treatment of Subacute Bacterial Endocarditis. Joseph C. Doane, M.D.

A short history of the development of heparin, together with its method of action, was given, in which the credit for originating this drug was assigned to Howell and his colleagues at Johns Hopkins University in 1916. The uses to which this drug have been put were stated as being: as an anti-coagulant in vascular surgery; for the prevention of post-operative pulmonary thrombosis; in blood transfusions; and in the treatment of subacute bacterial endocarditis. Three cases were reported as follows:

A mechanic, age 46, admitted to the service of the speaker on January 1st, complaining of chills and fever. Extraction of three teeth three weeks before admission was noted. A bacteremia, embolic phenomena and heart disease were present. Heparin and sulfapyridine treatment were given according to the method of Kelson and White. Death occurred on the sixth day of treatment, from massive cerebral infarction.

A female of 31, admitted to the same service on February 12th with a history and physical signs of a probable congenital septal defect with a bacteremia and embolic phenomena. Sulfapyridine and heparin treatment was given with apparent good response, but after eight negative cultures, positive cultures were again secured. The patient is now again under treatment.

A third patient, female, of thirteen years, admitted to the same service on January 27th with a history of chorea and with rheumatic symptoms on admission. Treatment was given, 330,000 units of heparin being administered together with sulfapyridine. In the course of the treatment a staphylococcus aureus septicemia ensued which responded to drainage of a labial abscess and the administration of sulfamethylthiazol. Many negative cultures, a flattening of the sedimentation rate, a gain of ten pounds, led the writer to believe that a cure had resulted.

6. The Use of Citrated Plasma in the Treatment of Secondary Shock. Max M. Strumia, M.D., Joseph A. Wagner, M.D., and J. Frederick Monaghan, M.D.

In the mechanism of shock production, progressive loss of circulating blood volume plays a major role. Because of the protein content, and the consequent high colloidal osmotic pressure, blood plasma administered intravenously has proved to be an ideal means of restoring an adequate blood circulation in patients suffering from secondary shock, rapidly relieving the clinical manifestations.

Blood plasma is readily obtained from citrated blood by the simple process of centrifugation and removal by suction in a closed system. It can be pooled and stored for use after the necessary serological tests for syphilis are carried out.

In institutions where a blood bank is in operation, plasma may be separated from the blood specimens on expiration of the maximum period of preservation, preferably five days.

Blood plasma offers the following advantages over whole blood: 1. It can be safely transported; 2. It can be stored for an indefinite period of time; 3. It is entirely safe and free from reactions; 4. It can be used in large and repeated doses; 5. It is instantly ready for use, typing and cross-matching being unnecessary; 6. It does not add to erythrocytes concentration if present.

7. Boeck's Sarcoid. David A. Cooper, M.D.

A group of cases was presented, showing the various manifestations of Boeck's sarcoid in which the diagnosis was proven by biopsy; the development of our knowledge of the condition was briefly reviewed: the earliest descriptions were of skin manifestations, which were known under a wide variety of names—later these skin lesions were associated with lesions in the lymph glands, bones and lungs. Stress was laid on the concept that Boeck's sarcoid is a generalized disease with many and varied manifestations.

Clinically the disease suggests a low-grade infection with mild toxemia. It is usually of long duration, often persisting for years, sometimes spreading from one organ or tissue to another, frequently relapsing, seldom producing serious constitutional symptoms, resistant to treatment, but at times healing spontaneously.

Clinical manifestations other than skin lesions, lymph gland lesions, bone and lung lesions, are the presence of a monocytosis during the active phase of the disease, and an increase in the total serum protein, which is usually due to an increase in the globulin fraction.

Pathologically, the lesions are similar wherever found, and they appear as a collection of large pale-staining epithelioid cells simulating tubercles. The characteristic features are the absence of caseation and of inflammatory reaction in the surrounding tissue. Giant cells of the Langhans type may be found.

The diagnosis cannot be proven without biopsy, but may occasionally be made by exclusion when the physical and roentgen findings are characteristic.

In the author's opinion the evidence presented in the literature to prove the tuberculous etiology of this disease is inconclusive, and the disease should be considered reticulosis of unproven etiology.

8. Sarcoid Disease, with a Review of Modern Concepts of Tissue Immunity. Carmen C. Thomas, M.D.

The various systemic manifestations of sarcoid disease have been described in the

literature since Besnier's original report of lupus pernio in 1889. Schaumann first correlated all of the diverse clinical manifestations under the collective heading of lymphogranulomatosis benigna.

This is a systemic disease characterized by circumscribed collections of epithelioid cells, interspersed with few giant cells and very little lymphocytic tissue response. It tends to involve the reticulo-endothelial apparatus particularly, produces relatively few symptoms, and is rarely fatal. Almost all organs of the body have been reported involved at one time or another. The eventual outcome may be disappearance of the sarcoid lesions with development of "classic tuberculosis" or a slow involution with fibrosis.

The etiology is as yet unestablished: tuberculosis, lepra, syphilis, and virus agents have been postulated. The circumstantial evidence favors a tuberculous etiology in many cases. Experimental production of sarcoid lesions has been accomplished by injections of phosphatid fractions of the tubercle bacillus (Sabin), by injection of attenuated tubercle bacilli into susceptible animals (Smithburn), and by virulent bacilli into immune animals (W. Jadassohn). Non-acid-fast variants of the tubercle bacillus have been isolated from sarcoid lesions in negroes (Mellon and Beinhauer).

The phenomenon of anergy to tuberculin has been reported in a preponderance of sarcoid patients in Europe and the U. S. A., but does not generally obtain in the case of sarcoid disease in the American negro. The presence of tuberculin weakening substances (anticutins) found by Martenstein and W. Jadassohn in the blood serum of sarcoid patients has not been generally confirmed by recent work, nor were such substances demonstrated in the tissue fluid from involved portions of the skin of such patients.

SECTION ON MEDICAL HISTORY

Regular Meeting, March 11, 1940

Richard Bright, Traveller and Artist.[1] Burton Chance, M.D.

Syphilis of the Skull among Aleuts, and the Asian and North American Eskimo about Bering and Arctic Seas.[2] Richmond C. Holcomb*, M.D., Capt., M.C., U.S.N., *Ret.*

The Medical Guilds. Edward F. McLaughlin*, M.D.

Regular Meeting, April 8, 1940

Gleanings from Old Chinese Medicine. Bernard E. Read*, M.D.

Paul Ehrlich and His Relation to Modern Chemotherapy.[1] Maurice S. Jacobs, M.D.

Regular Meeting, May 13, 1940

Prolegomena to the Life and Works of Ugo Benzi (1376–1439).[3] Dean P. Lockwood*, Ph.D.

The Old Philadelphia Laryngological Society of the Eighteen-eighties. Meyer Solis-Cohen, M.D.

SECTION ON OPHTHALMOLOGY[4]

Regular Meeting, March 21, 1940

On the Intravital Colour of the Macula. J. W. Nordensen*, M.D.

Glaucoma, Analysis of Pathology. T. L. Terry*, M.D.

[1] This paper is scheduled for publication in the *Bulletin of the History of Medicine.*

[2] Printed in the *United States Naval Medical Bulletin*, April 1940, **38**: 177–192.

* *By invitation.*

[3] Printed in this (June, 1940) issue of the *Transactions & Studies.*

[4] The transactions of this section are abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology.*

Regular Meeting, April 18, 1940

Hand-Schüller Christian Syndrome: a Case Report. Eunice Stockwell*, M.D.

Primary Pituitary Adenomata and the Syndrome of the Cavernous Sinus. Francis C. Grant, M.D., and Laurence M. Weinberger*, M.D.

Congenital Colobomata of Both Both Lower Lids. Edmund B. Spaeth, M.D.

SECTION ON OTOLARYNGOLOGY[5]

Meeting, March 20, 1940[6]

Endaural Fenestration of the Horizontal Semicircular Canal for Otosclerosis. Julius Lempert*, M.D.

* *By invitation.*

[5] The transactions of this section are abstracted in the *Archives of Otolaryngology*.

[6] Joint meeting with the Section on Otolaryngology of the New York Academy of Medicine, held in New York.

Regular Meeting, April 17, 1940

Case of Mastoiditis with Recovery Only after Rupture of Possible Retropharyngeal Abscess. H. A. Rothrock, M.D.

Laryngectomy for Intrinsic Cancer of the Larynx (Subperichondrial Extirpation of the Larynx). Gabriel Tucker, M.D.

Laryngectomy by Local Anaesthesia. Robert E. Buckley*, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

Meeting, April 29, 1940

Symposium on Philadelphia's Water

The History of Our Water Supply. Seth M. Van Loan*.

Plans for Immediate Improvements. Nathan B. Jacobs*.

Quantity, Quality and Finances. Charles A. Howland*.

Notes from the Library, the Mütter Museum, and the Committee on College Collections

The Library

A NEW LIBRARY FUND ("Fund of the Friends of George E. Pfahler").

At the meeting of the college on May 1, 1940, Dr. Eugene P. Pendergrass, who fathered the idea of establishing a library Fund of the Friends of George E. Pfahler, in the following words formally presented the Fund, on behalf of Dr. Pfahler's friends:

On January 25, 1940, a large group of friends of George E. Pfahler held a dinner in honor of that distinguished Philadelphia physician, who, a pioneer in the use of the Roentgen-rays, has contributed so notably to the development of their use in medicine.

The occasion was a memorable one. After the dinner, it was found that the contributions of Dr. Pfahler's friends had been so numerous and generous that a considerable sum remained in the hands of the committee. It was felt that this sum could very properly be devoted to the creation of a permanent form of tribute to Dr. Pfahler. The friends agreed that a fitting form for this to take would be a fund for the purchase of roentgenological literature for the library of the College of Physicians, of which Dr. Pfahler has been a Fellow for thirty-five years. The Philadelphia Roentgen-Ray Society contributed a sum sufficient to raise the principal to $1000; Dr. Pfahler himself, when he learned of our plan, generously reciprocated the tribute from his friends by adding a thousand dollars.

And so it is my privilege to present to the College this cheque for two-thousand dollars, for the establishment of the Fund of the Friends of George E. Pfahler, believing that in this way our memory of an occasion, and of a man we wished to honor, will be appropriately preserved for as far into the future as we can see.

RECENT ACQUISITIONS

From *Dr. P. Brooke Bland*, whose collection of medical *rariora* is well known to those interested in the study of medical history, have come the following important works in beautifully preserved condition:

Bohn, Johannes. Circulus anatomico-physiologicus, seu Oeconomia corporis animalis. Leipzig, Fritsch, 1697.

Garrison says that Bohn "experimented upon the decapitated frog (1686) in an entirely modern spirit, declaring the reflex phenomena to be entirely material and mechanical, as against the current view of 'vital spirits' in the nerve-fluid. . . . Bohn showed that the pancreatic juice is not acid and that the nerves do not contain a 'nerve-juice'."

As the number of text pages in this edition corresponds almost exactly with that given for the Leipzig edition (different printer) of 1686, it may be assumed that the chief difference between the editions is a more extended index in the later one. Haller refers to a 1680 edition, which, if it exists, must lack the material on the experiments referred to above.

Cocchius, Antonius. De usu artis anatomicae oratio. Editio secunda cui accedunt Observationes ad lithotomiam attinentes aliaque Chirurgiae monumenta auctore. . . . Gulielmo Bromfeild. Florence, Bonduccius, 1761.

This rare volume (it is not listed in the Index-catalogue of the Army Medical Library) is of considerable interest. Antonio Cocchi, Florentine professor of anatomy, was one of the more enlightened physicians of the first half of the 18th century, publishing works on anatomy, surgery and other branches of medicine, as well as leading in the introduction of prophylactic legislation against tuberculosis. He traveled to England with Lord Hastings and became the friend of Isaac Newton and Richard

Mead. The *Oratio* here reprinted (first published in 1736) is, in effect, a brief and lucid history of anatomy. It may be observed that, though he is well aware of the contributions of Colombo and Cesalpino to the subject, he says (p. 30), "We freely yield the glory of this discovery [i.e., of the circulation of the blood] to a Briton, who made it clear in all respects, and manifest, and who explained with great clarity the application of this discovery to the life of man and of all living things, and to an understanding of nature."

William Bromfield's pretensions to eminence in the history of surgery have been rather mercilessly dealt with by G. C. Peachey (*Proc. Roy. Soc. Med.*, Sec. Hist. Med., 1915, **8**, pt. 2, 103–125; *also*, Janus, Leyde, 1916, XXI, 27–50), among them his invention of "Two lithotomical instruments, one a *bistourie caché*, to divide the neck of the bladder, and the other, a double gorgeret, for cutting through the prostate gland, for which latter instrument he claimed greater safety and other advantages over the much better known 'cutting gorget', which is traditionally associated with the name of his rival, Caesar Hawkins, and was then used by almost every surgeon in England who operated for lithotomy."

Peachey's list of Bromfield's published works fails to mention, singularly enough, a description (illustrated), in French, of the double gorgeret, and of its use, published under Bromfield's name in Vandermonde's *Journal de medecine, chirurgie, pharmacie, etc.*, 1761, **14**: 68–73. As Bromfield's son, William Heriot Bromfield, published in the same year a French translation by himself of his father's "Account of the English nightshades," it may safely be assumed that the translation of the description also was his. The same volume of the *Journal* contains *Reflexions* on the Bromfield memoir by the Florentine surgeon Michelangelo Grima (p. 161), and an anonymous *Avis* (p. 559) correcting a few of the directions given in the memoir.

We cite this omission principally because it has a bearing on our new acquisition. The Bromfield "Observations" which it contains include most of the *Journal* description, in somewhat altered form, as well as much more material not up to that time published by Bromfield. There are present, also, the Grima *Reflexions*, now in Italian, and acknowledgedly extracted from the *Journal;* the *Avis*, likewise become *Avviso*, which the publisher claims was received by Angelo Nannoni as a letter from William Bromfield *fils;* a reproduction of the *Journal* plate illustrating a four-branch lithotomy forceps holding a stone, and the double gorgeret.

What this sequence of events shows, then, is the pious activity of a son on behalf of a father who has given him early advantages which he never himself enjoyed. William Heriot Bromfield attended Eton, obtained a medical degree at Padua, studied in Florence with the illustrious Professor Cocchi, became a member of the Academies of Botany of Cortona and Florence, and of the Royal Academy of Science at Paris, before dying, in 1762, at the early age of twenty-six. We may assume that he negotiated the publication in French of the description of his father's inventions; elicited the *Riflessioni* from Sig. Grima, who begins by saying that the younger Bromfield has loaned him his father's instruments; prepared the Latin version of his father's observations and possibly arranged for its publication in Florence, along with Grima's *Riflessioni* and the corrective *avviso*. Certainly it is not without some significance that the publisher dedicates the volume rather fulsomely to this talented and enterprising young Britisher, and unites with the father's work one by the son's Florentine preceptor, Antonio Cocchi, who had died three years before. One is inclined to wonder if the scene of the transaction was not illumined by a discreet display of Bromfield silver. However that may have been, the medical world gained a volume of considerable interest; William Bromfield, the eminent, if continually embattled, surgeon, lost in the following year a son whose talents and filial devotion might have refined the edges of the older man's eccentricities—though, of course, it might have worked out the other way round.

Scarpa, Antonio. Atlante delle opere complete . . . e spiegazione delle tavole che lo compongono. Volume unico. Firenze, Batelli, 1839.

The collected works of this great and versatile surgeon and anatomist (1752–1832) were brought out, 5 parts in 2 volumes, in Florence, 1836–8. The separately-published atlas here listed is related to that edition. Though the library has a number of the original editions, it contains only part 4 of the collected edition; thus, this atlas fills a real gap, supplying as it does the illustrations to texts which we must hope to acquire at some future time.

Hemsterhuis, Siboldus. Messis aurea exhibens; anatomica: novissima et utilissima experimenta. . . . Huic editioni accesserunt de vasis lymphaticis tabulae

Rudbeckianae . . . Heidelberg, Wyngaerden, 1659.

The stir created by the almost simultaneous discoveries of Jean Pecquet (1651), Olof Rudbeck (1653), and Thomas Bartholinus (1654), amplifying and correcting the discovery of the lacteal vessels by Aselli, is suggested by the publication, in 1654, of two collections uniting the work of Pecquet and Bartholinus. At Genoa, Johannes Alcidius Munierus edited a reprint of Pecquet and Bartholinus; at Leyden, a young medical student, Sibout Hemsterhuys, brought together the pertinent works of Pecquet, Bartholinus, and Rudbeck; both of these long ago found their way into the library. The latter collection appeared in this second edition, five years later, at Heidelberg, much handsomer, and enriched by a dozen or so additional plates illustrating the Rudbeck treatises.

John Hunter Letter. From the same generous donor came also the following letter, dated June 7th 1791 at Leicester Square, sent by John Hunter to "General The Marquis Townshend": "Mr. Tudor having acquainted me that he has agreed to purchase Mr. Gavin Hamilton's Commission as Surgeon to the 2d. or Queen's Regiment of Dragoon Guards under Your Lordship's Command, who is allowed to sell having purchased the same: I beg leave to inform Your Lordship that I look upon Mr. Tudor, who has been duly examined at Surgeons-Theatre, to be properly qualified in his Profession, and a fit Person to become the Purchaser." P. S. Mr. Tudor got the commission (See Plarr's "Lives," vol. 2 (1930), p. 440) by purchase on May 25, 1791.

Dr. Charles W. Burr, that incomparable friend of the library, has enriched our collection of primary source material by two notable gifts.

1. Andreas Caesalpinus. Quaestionum peripateticarum lib. V; Daemonum investigatio peripatetica; Quaestionum medicarum lib. II; De Medicament. facultatibus lib. II. Venice, Junta, 1593.

Of the various European claimants to Harvey's title of discoverer of the greater circulation, perhaps Cesalpino is the best supported. Osler said that an excellent case can be made out for him on the evidence contained in these works. Through some unknown combination of circumstances, contemporary texts of these works, of prime importance in the history of medicine, have not hitherto been available to scholars coming to work in this library. The want has more than once been felt, and there is great satisfaction that it has at last been met.

2. Jean Pecquet. New anatomical experiments . . . London, T. W. for Octavian Pulleyn, 1653. (Bound with:) Thomas Bartholinus. The anatomical history . . . concerning the lacteal veins of the thorax . . . London, Francis Leach for Octavian Pulleyn, 1653.

These are the very rare and much prized English translations of the Pecquet and Bartholinus works referred to above in connection with Dr. Bland's gift of the Hemsterhuys collection.

Dr. Burton Chance, at the March meeting of the Section on Medical History (and subsequently at the annual meeting of the American Association of the History of Medicine) read an interesting paper entitled "Richard Bright, Traveller and Artist." Many may have become thereby acquainted for the first time with a little-known side of that great English clinician and pathologist's life. Dr. Chance's "Exhibits A and B" were the following two works, which he presented to the College library at the April meeting of the College. Readers are referred to Dr. Chance's paper, scheduled for publication in the *Bulletin of the History of Medicine*, for a full account of these rare and interesting volumes.

1. Richard Bright. Travels from Vienna through Lower Hungary; with some remarks on the state of Vienna during the Congress, in the year 1814. Edinburgh, 1818.

2. Sir George Steuart Mackenzie, Bt. Travels in the island of Iceland, during

the summer of the year MDCCCX. Edinburgh, 1811. (Contains chapters on botany and zoölogy by Richard Bright.)

Dr. Thomas S. Githens has contributed to our collection of early alchemical works the following:

Michael Sendivogius. Chymische Schrifften. Vienna, 1750.

Sendivogius (1566–1646), one of that fabulous group of seekers after the Philosopher's Stone, left scarcely any authenticated writings. Nevertheless, a published corpus sendivogium came into being and is here represented. An English translation of the most famous of the works falsely attributed to him, "The new chemical light," will be found in volume 2 of "The Hermetic museum" (London, 1893), a copy of which was acquired by the library two or three years ago. Our new volume contains at the end a manuscript transcription of an Amsterdam, 1606, edition of "Der verlangete dritte Anfang der Mineralischendinge, oder dem philosophischen Saltz," ascribed to the "Sohn Sendivogii genant J. F. H."

The Mütter Museum

RECENT ACQUISITION

A case of instruments taken from a German storehouse in 1917. Gift of Hubley R. Owen, M.D.

The Committee on College Collections

The Committee reports the completion of the new catalogue of college collections, and the following recent acquisitions:

A case of cupping instruments, and a lancet. Gift of Alexander Randall, M.D.

A "Pap Boat," a small china dish used in the feeding of infants about 1790 or 1800. Gift of John Frazer, through E. B. Krumbhaar, M.D.

A "Pap Spoon," used in the feeding of infants about 1800. Gift of E. B. Krumbhaar, M.D.

Bronzed plaster busts of Hippocrates and Dupuytren. Gift of Ludwig Loeb, M.D.

A case containing three old-fashioned craniotomy instruments. Gift of Ludwig Loeb, M.D.

A photograph of the president, Dr. Krumbhaar, the vice-president, Dr. Pepper, and the secretary, Dr. Austin, on the dais in Mitchell Hall, taken by F. William Sunderman, M.D. Gift of Dr. Sunderman.

Three instruments formerly belonging to John H. Girvin, M.D. Gift of Miss Helene Girvin.

Three boxes of microscopic slides. Gift of Simon S. Leopold, M.D.

Schedule of Scientific Lectures, 1940-1941

*September 25, 1940.** To be announced later. (*Nathan Lewis Hatfield Lecture XXIV.*)

November 6, 1940. John F. Fulton, M.D. Functions of the Frontal Lobe. (*S. Weir Mitchell Oration VIII.*)

December 4, 1940. Allen O. Whipple, M.D. Recent Studies in the Circulation of the Portal Bed and of the Spleen in Relation to Splenomegaly. (*Thomas Dent Mütter Lecture LIII.*)

January 8, 1941. Thomas Francis, Jr., M.D. The Problem of Epidemic Influenza. (*James M. Anders Lecture XVI.*)

February 5, 1941. Thomas T. Mackie, M.D. Ulcerative Colitis. (*Mary Scott Newbold Lecture XLVIII.*)

March 5, 1941. Ernest W. Goodpasture, M.D. The Cell-Parasite Relationship in Bacterial and Virus Diseases. (*Alvarenga Prize Lecture.*)

April 2, 1941. George L. Streeter, M.D. Embryology of the Human Ovum. (*Nathan Lewis Hatfield Lecture XXV.*)

May 7, 1941. Henry F. Vaughan, M.D. The Way of Public Health. (*James M. Anders Lecture XVII.*)

* Advanced from October 2, to prevent conflicting with the annual session of the Medical Society of the State of Pennsylvania, to be held in Philadelphia, September 30 to October 3.

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 8 (Fourth Series)

Number 3 (December 1940)

Neurology and War*

By J. F. Fulton, M.D.

Laboratory of Physiology, Yale University School of Medicine

I. INTRODUCTION

MEDICINE is probably the only non-belligerent profession in which progress has been made as the direct result of war, and the challenge of war to the physician is perhaps greater than that to any other member of society. Since so little of enduring value is likely to emerge from armed conflict, it becomes the duty of every physician to snatch from the chaos of belligerency anything, however slight, that may be of permanent worth. If English-speaking peoples emerge free after the present world struggle and continue to carry on with a few of the traditions of civilization, the conflict surely will not have been in vain. But it is not for the physician to waste time on these larger issues; rather should he go about his business of healing the wounded, preventing pestilence and seizing upon every opportunity to advance his art, being thankful meanwhile that he is at liberty to pursue his calling.

The opportunity to study human physiology and pathology in the gigantic laboratory created by a theatre of war is one that is seldom fully grasped. It is a national opportunity and requires national organization adequately to cope with it. Shall we be farsighted enough to plan studies in advance, to see that similar material is grouped together and followed by those best qualified to analyze it; will records be kept of the vast experience so that those in later years will be able to profit by what we have learned; and, finally—since it is a truism of experimental medicine that the chronic experiment yields far more precise knowledge than the acute—shall we this time see to it that the individual wounded man is followed and remains followable until his death?

In less metaphorical language, one may properly ask whether the American medical profession is ready to accept the

* Weir Mitchell Oration VIII, The College of Physicians of Philadelphia. This paper was scheduled to be read at a Scientific Meeting of the College on November 6, 1940. The meeting was not held, owing to Dr. Fulton's inability to return from England in time to be present. The Publication Committee and the editor are grateful to Dr. Fulton for preparing the paper for publication in the midst of many pressing obligations.

challenge of the present emergency: namely, *to study the wounded man*, in addition to sewing him up or setting his fracture; to segregate similar cases on a national scale, to coöperate to the fullest possible extent with all government services and agencies responsible for the sick and wounded; and lastly, have we the vision to develop a follow-up system that will work throughout the life of the patient, one which will lead automatically to an autopsy? My impression is that our thinking in these lines is as yet somewhat superficial. Let us get down to it before it is too late, for we shall ultimately be judged by our foresight at the present moment. In England there was planning on these lines before the war started, but not on a national scale. Our medical colleagues in Britain have moved swiftly, and have salvaged much, but not as much as we can salvage if we have the wisdom now to profit by their experience, their difficulties, reverses, failures and successes. Our capacity to do these things depends in the first place upon the initiative of the profession; secondly, upon the support of the government.

Many phases of medicine in the past have been advanced during wars, but none more conspicuously than neurology. I have chosen the subject neurology and war because it seemed especially fitting for an oration bearing the distinguished name of Weir Mitchell (1829–1914)—one who at an early age accepted the challenge of war. It was as a military surgeon that Weir Mitchell achieved his principal early successes. He had entered the Union Army as a surgeon at the beginning of the Civil War, and he became distinguished almost immediately for his surgical skill as well as for remarkable acuity in clinical observation. There is a rare and little-known pamphlet issued as "Circular, No. 6" from the Surgeon-General's Office, dated March 10, 1864, which is signed by Weir Mitchell, G. R. Morehouse[1] and W. W. Keen (Fig. 1). This seventeen-page pamphlet bore the title *Reflex paralysis*, and it formed the basis of a book, published later in the year by the same authors, entitled *Gunshot wounds and other injuries of nerves*, one of the first great classics in the history of American surgery.[2]

The circular and the book itself are noteworthy today, for Weir Mitchell was the first to approach battle injuries in the light of the newer physiology. He had had the opportunity of studying in 1850–51 under Claude Bernard; he was therefore fully familiar with the important French work on vasomotor reflexes, and we find him constantly

[1] W. W. Keen requires no comment for he later became one of the foremost figures of American surgery. Morehouse was more obscure. He had collaborated with Mitchell in their celebrated *Researches upon the anatomy and physiology of respiration in the Chelonia* published by the Smithsonian Institution in 1863. Of their association during the Civil War Mitchell himself writes: "Early in the Civil War Dr. Morehouse served in the Filbert Street Hospital as assistant surgeon under contract. When the Hospital for Nervous Diseases was organized I asked to have him as my colleague. Then Dr. William W. Keen joined us and we remained in useful co-partnership of labor up to 1865.

"During our long service he operated often and had the skillful hand, the ready decision of the moment, and the courage which might have made him a surgeon of distinction. I recall two instances of his capacity. In one desperate case of paralysis he removed through the mouth a bullet which had lodged in the cervical vertebrae. The patient recovered. I saw him trephine the skull and open a cerebral abscess, the first case I believe on record unless one by Detmold preceded it." (Kelly, H. A., and Burrage, W. L., *American medical biographies*, Baltimore, 1920 [see p. 815].)

[2] See also Mitchell's *Injuries of nerves and their consequences*, 1872, and *Lectures on diseases of the nervous system, especially in women*, 1881.

referring to Bernard's physiological experiments in interpreting conditions of syncope, shock and various forms of central and peripheral motor paralysis. experiments, in which he showed that irritation of the posterior roots of spinal nerves suddenly checks the cardiac motions for a time, and that like irritation

Circular, No. 6.

Surgeon General's Office,

WASHINGTON, D. C., *March* 10, 1864.

The following paper on Reflex Paralysis, the result of gun-shot wounds, founded chiefly upon cases observed in the U. S. General Hospital, Christian Street, Philadelphia, by S. WEIR MITCHELL, M. D., GEORGE R. MOREHOUSE, M. D., and WILLIAM W. KEEN, Jr., M. D., is published for the information of Medical Officers, in the belief that immediate and practical benefit may be derived from it.

JOS. K. BARNES,
Acting Surgeon General.

Since the establishment, in May, 1863, of a Special Hospital for the treatment of diseases and injuries of the nervous system, a vast number of cases of gun-shot and other injuries of nerves have been studied by the authors of this paper.

The great mass of these will be considered in a future essay, upon the history, results, and treatment of gun-shot wounds of nerves. We have judged it wise, however, to report separately a class of very infrequent cases, in which paralysis of a remote part or parts has been occasioned by a gun-shot wound of some prominent nerve, or of some part of the body which is richly supplied with nerve branches of secondary size and importance.

So far as we are aware, the Medical Histories, which we are about to record, stand alone as the first reports of sudden reflex paralysis from mechanical injuries. How they differ from the paralytic affections which result from disease of organs, and which have been so ably treated of by numerous authors, we shall presently consider. That they have thus far escaped notice may be easily accounted for. In the first place they are rare; among some sixty or more carefully studied instances of wounds of nerves, we have met with only seven cases of reflex paralysis of remote organs, in which the influence was prolonged or severe. In the majority of cases, the reflex effect is either very slight or very transient, and for one or both of these reasons, unlikely to attract notice from surgeons on the battle-field, or in Division or Corps hospitals, where their brains and hands are taxed to the utmost, by the palpable misery of wounds in the early stages of treatment. Had it been otherwise, we do not doubt that numerous cases of reflex paralysis from injuries to nerves would have been recorded

FIG. 1

Thus in the circular he says (p. 2): "In fact it has long been known that the sudden crushing of a limb in inferior animals will stop the heart or make it act slowly for a greater or less length of time. Now if we add to this M. Bernard's of the anterior or motor roots gives rise to no such result, we shall be able to see how it is possible that a gun-shot wound of a large limb may be competent to effect a like result."

During the past few months I have had

the privilege of studying the deliberations of our National Research Council Committee on Shock and have also recently attended a meeting and studied the earlier minutes of the Medical Research Council's Committee on Shock in England. Neither Committee to date, so far as I am aware, has considered the part played by the central nervous system in shock; yet in the Circular of March 10, 1864, one finds the following passage on page 3 which suggests that Weir Mitchell and his colleagues were nearly a hundred years ahead of their time:

> The majority of physicians will no doubt be disposed to attribute the chief share in the phenomena of shock in its various forms, to the indirect influence exerted upon and through the heart. There are, however, certain facts, which duly considered, will, we think, lead us to suppose that in many cases the phenomena in question may be due to a temporary paralysis of the whole range of nerve centres, and that among these phenomena the cardiac feebleness may play a large part, and be itself induced by the state of the regulating nerve centres of the great circulatory organ.
>
> The loss of consciousness, and the appearance of a state outwardly resembling syncope, prevent us in most cases from feeling sure that the great nerve centres suffer loss of function primarily and not through want of nutrition from feeble or arrested heart action. But there do exist certain cases, more rare it is true, in which singular affections of the nerve centres, other than those of the heart, occur as a consequence of wounds.

There is a curiously familiar ring about these two paragraphs, and anyone who has witnessed the casualties from present-day bombing or who has studied the endless deliberations about the best way of handling those cases which show no visible external wounds (but which nevertheless exhibit all the classical symptoms of shock), will realize that Weir Mitchell saw far more deeply than many of his contemporaries and in some respects more deeply than those who have cared for the wounded in the two world wars which followed his death in 1914.

In reading the circular and the later book on gunshot wounds, one can find passage after passage in which views are expressed differing in no essential regard, except diction, from similar views now being expressed in the minutes of our National Research Council Committees on brain injuries, shock, injuries of peripheral nerves, etc. But despite all this, the present war has already brought notable progress in neurology, and I would like briefly to mention several neurological topics drawn from recent English sources.

II. SHOCK AND THE CENTRAL NERVOUS SYSTEM

In support of his belief that states of shock accompanied by loss of consciousness without external wounds might be due to derangement of the central nervous system, Weir Mitchell and his colleagues cited a number of instances of soldiers who were found collapsed (some were also hysterical), but without external injury, as a result of proximity to an exploding shell. He also mentioned the case of a pharmacist who had been knocked over by an explosion of ingredients he was mixing with his mortar and pestle and who had all the classical symptoms of circulatory collapse, although he had not actually struck his head after the explosion.

In England at the present time much perplexity has been felt over the fact that individuals are frequently found dead in the vicinity of a bomb explosion, even though they have not been struck by shrapnel or débris. Others more distant from the site of the explosion are often picked up in a state of profound circulatory collapse without visible sign of injury. The first autopsy report of

death from primary blast (ten cases) has appeared in the *Lancet* for October 19, 1940, under the authorship of Geoffrey Hadfield and his colleagues. All ten cases showed some degree of injury to the lungs. In five in which the brain was examined there was no gross damage except for subpial extravasation of blood in one instance. In two instances the injury to the lungs was probably sufficient to have accounted for death; in three other cases death was obviously caused by carbon monoxide poisoning, due no doubt to the rupture of gas mains incident to the bombing explosion. The data presented in this preliminary report of ten cases are meager, but emphasize that proximity to a high explosion may cause death, even though histological changes in the lungs and other tissues are relatively insignificant.

An experimental analysis of the problem was reported on August 24 by Zuckerman, also in the *Lancet*. He had studied the effect of high explosive charges on monkeys placed at varying distances from the site of the explosion. The physical wave of pressure created by such an explosion has a high velocity initially, but falls off rapidly. Thus at 15 feet from the wave the hydrostatic pressure may be of the order of 200 lb. per square inch, whereas 50 feet away the maximum pressure may not be more than 10 lb., in excess of the normal 15 lb. per square inch of atmospheric pressure. At 15 ft., therefore, the body and the lungs are exposed to a violent pressure-wave, moving at a rate sufficient to give the body an acceleration many times that caused by the action of gravity, whereas at 50 ft. the pressure-wave will only be from 2 to 3 times that of sea-level atmospheric pressure. All things in the immediate neighborhood of an explosion will thus experience a violent increase of wind velocity and hydrostatic pressure which may be of sufficient intensity to carry a human body far from the scene of the explosion. Zuckerman's results with animals may be summarized in his own words:

> These experiments were carried out on mice, rats, guineapigs, rabbits, cats, monkeys, and pigeons, and were of two kinds. In the first animals were exposed at various distances to blast from 70 lb. of high-explosive placed (in paper containers) on the ground; in the second animals were exposed to blast from the explosion of charges of hydrogen and oxygen in balloons In both, blast pressures were measured by means of piezo-electric gauges, and the experiments were so arranged that there were no flying missiles (e.g. stones) to hurt the animals. . . .
>
> The closest an animal was placed to the charge in any experiment was 13 ft., and the furthest 70 ft. No animals were ever killed at distances further than 18 ft. and none was hurt in any observed way at distances further than 50 ft. from the explosion, a distance at which the positive component of the blast wave was of the order of 6.3 lb. per sq. in. and the suction component 1.3 lb. per sq. in. Between 13 and 18 ft. almost all animals were killed when placed so that their body walls were affected by hydrostatic pressure alone (i.e., end-on to the charge). At these distances the positive component of the blast wave (hydrostatic pressure) varied between 126 and 63 lb. per sq. in.
>
> Between 20 and 50 ft. no animal was killed, and with few exceptions all animals which survived showed little or no change in behaviour. Most were quieter than they had been before the explosion, and except in marginal cases all ate readily when fed immediately afterwards. Animals at 20 ft. and those that survived at 18 ft. often breathed irregularly and showed signs of respiratory embarrassment.
>
> In none of the animals was there any external sign of injury, and in no case were fractures observed. The most outstanding lesion (as found by Hooker) was bilateral traumatic haemorrhage in both lungs varying in degree according to the distance of the animals from the charge. Occasionally lesions have been found in other organs (e.g. liver, intestine). . . .

Autopsies on cases of death from blast and Zuckerman's analysis of blast

in animals thus indicate that some factor in addition to pulmonary damage plays a part in causing collapse or death in bombing casualties. Highly important data bearing upon this problem have come from Denny-Brown and Russell. They find, contrary to previous beliefs, that cerebral concussion results, not from the intensity of the blow on the head, but from *sudden acceleration resulting from the blow.* In conversation Denny-Brown mentioned a case that had come recently to his attention of a mechanic who had been under an automobile with his head solidly on the ground. The machine fell off the jack and the differential suddenly pinioned his head against the ground, giving him a severe compound fracture of the skull. The man suffered no loss of consciousness and experienced none of the symptoms of concussion. There had been no acceleration of the head.

If, however, the head is struck when unsupported and is thus able suddenly to move, symptoms of concussion inevitably develop, and it is striking in this connection that a high velocity shell fragment may actually pass completely through a man's skull without causing loss of consciousness, or his even being aware that anything had happened, the size and velocity being such that it gives no acceleration of movement to the head itself. *De-acceleration* is similarly effective in producing concussion; *i.e.*, if a movement of the head in any direction is abruptly stopped, concussion results. On the basis of these *a priori* arguments Denny-Brown and Russell have contrived an ingenious pendulum for producing blows on the head of a lightly anesthetized animal. The head is so placed that it is free to move when struck by the falling pendulum. The mass of the pendulum is greater than that of the head itself. Symptoms of concussion failed to appear when the blow was struck at a velocity of less than 20 ft. per second. With higher velocities, *i.e.*, between 20 to 30 ft. per second,[3] the following symptoms occur usually in this sequence.

(i) *Shock.* When the blow is delivered at about 23 to 24 ft. per second the animal develops the classic symptoms of traumatic shock. The pulse rate slows for a time and then increases, blood pressure falls, respiration becomes quick and shallow, and the animal becomes incapacitated for a period of several hours; but reflexes such as the knee jerk, the pinna and corneal reflexes are unaffected. It is highly significant, especially in view of Zuckerman's work on blast, that a blow on the head can of itself induce symptoms of generalized shock. The air blast from an exploding bomb is quite capable of causing a sudden acceleration of the head; indeed the whole body may be suddenly lifted at a high acceleration, and this would be sufficient to account for the circulatory collapse caused by proximity to a bomb explosion.

(ii) *Concussion.* Denny-Brown and Russell make distinction between shock as such, and symptoms of concussion which develop when slightly heavier blows are delivered, *i.e.*, those struck at a velocity of 25 to 28 ft. per second. Following these heavier blows the corneal and pinna reflexes are abolished for varying intervals; the resting posture (tonus) of the extensors disappears, and spinal reflexes may be altered or even temporarily abolished. A blow of this magnitude if delivered to a conscious animal would render it unconscious;

[3] It is not clear what acceleration, as measured in 'g,' this would give to the head. It would probably be of the order of 15 to 20 'g,' but no determination has yet been made of the cushioning effect of the scalp.

whereas the blow causing shock does not necessarily cause unconsciousness.

The pathological changes in the brain associated with shock and concussion blows have been carefully sought and have been proved wholly absent as far as ordinary microscopic examination is concerned. There are no petechial hemorrhages and no contused or hemorrhagic areas in the medulla or cerebral hemispheres. The microscopic causes for the symptoms of concussion are still obscure, but no doubt have to do with some basic intracellular disorganization of the neuron.

(iii) *Contusion.* When blows are delivered to the head at a rate greater than 28 ft. per second, contusions develop in which hemorrhages may occur beneath the site of the blow (or as a contre-coup at the opposite side of the head), and petechial hemorrhages are prone to develop, especially in the basal nuclei, brain stem and medulla. Animals exhibiting concussion plus contusion may die shortly after the blow is received, as Pilcher (1937) and others have already noted. If they recover, they become notoriously susceptible to further blows or to temporary failure of the circulation.

These studies obviously throw highly significant light upon the problem not only of injuries of the head *per se*, but on bombing and shelling injuries generally. They likewise indicate that generalized shock associated with bombing may emanate from some failure or disorganization, presumably in vasomotor control, on the part of the central nervous system, as Weir Mitchell originally suggested.

Another problem even more closely associated with Mitchell's name is that of peripheral nerve injuries.

III. PERIPHERAL NERVE INJURIES

Mitchell was much concerned how best to deal with severed peripheral nerves. He improved upon several well-known methods of nerve suture and his results were on the whole good, but these were before the days of antisepsis and the many infected nerve trunks and ganglia which developed in his cases led him to recognize a new syndrome of "Causalgia," of which he and his colleagues gave a classical description in *Gunshot wounds* (p. 78 *et seq.*). Apart from the introduction of antisepsis, however, there was little fundamental advance in the mode of suturing nerves until the advent of the present war.[4]

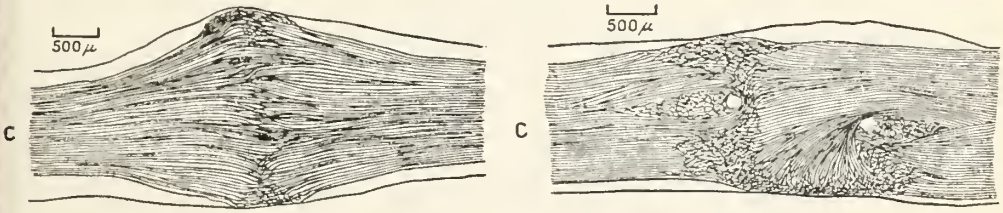

FIG. 2. Young and Medawar's diagram illustrating fibrin suture as compared with silk suture of the sciatic nerve of the rabbit. *Left*, junction made with plasma 25 days previously. Fibres have grown forward with little deviation except at the edges. *Right*, junction made with fine silk sutures. Note whorl production and deviation of bundles. (Reproduced, by permission, from *The Lancet*, Aug. 3, 1940, p. 127.)

[4] A full and interesting discussion of peripheral nerve surgery during the last war will be found in the monograph of Pollock and Davis, 1933. A discussion of the problem in relation to the present war has just been given by Cairns and Young (1940).

Now, thanks to the ingenuity of an Oxford zoölogist, John Z. Young, who has devoted many years to the study of structure and conduction in peripheral nerves, a new and highly effective method has been introduced for the reuniting of nerves, not by suture but by anastomosis with concentrated plasma solutions (See Young and Medawar, 1940). This method, which allows the plasma to clot around the stumps of the nerves, gives a much smoother and more physiological union without the serious distortion among nerve fasciculae which inevitably results from the use of silk sutures. Running a small cat-gut suture through a mixed nerve trunk is a little like pulling a two-inch rope through a silk brocade. The method and early results of the new procedure have been fully described by Mr. Young and his collaborators in a recent number of the *Lancet* (August 3, 1940). They find, among other things, that nerves regenerate more rapidly when sutured by fibrin, the rate in the rabbit being approximately 4 mm. per day after a latent interval of 8 days.

Another advance of peripheral nerve studies has come through the work of Woollard, Weddell and Harpman (1940) now being carried on by Weddell at Oxford. He has devised a means for intravitally staining nerve terminations in the skin. By his method it is possible to demonstrate when a sensory nerve has actually regenerated into the skin. Full details of this work have also been published in a recent number of the *Journal of Anatomy*.

With regard to management of cases of peripheral nerve injury during the period before physiological regeneration has occurred, there has been little advance since Weir Mitchell's time. Indeed, both in Britain and in this country, there is still sharp division of opinion whether massage or electrical stimulation should be instituted to diminish muscular atrophy. Recent clinical experience appears more favorable to massage, but electrical stimulation with slowly rising currents suitable for the prolonged chronaxie of degenerating skeletal muscle has not yet been adequately studied.

IV. CONCLUSION

Many other phases of neurology might be touched upon in a general address upon Neurology and War. There is the large field of head injuries, and the value from the point of view of functional localization of studying the effects of sharply circumscribed lesions. Notable additions to knowledge were made in the last war from works of this character by the late Sir Henry Head, Gordon Holmes, Cushing, and many others, but so far in this war there have been few circumscribed injuries. Present-day warfare is no longer a static conflict carried on in trenches where the head of a man was the part of his body most likely to receive injury. There have been head wounds in the present war—many of them—but it is probably not an exaggeration to say that the majority have resulted from motor accidents during blackouts. Many head injuries have also resulted from débris falling in the vicinity of a bomb explosion, and finally, large numbers of injuries have been caused by minute flying splinters. Surprisingly few of these have led to sharply circumscribed lesions of the brain, and it is improbable that there will be any considerable increase in such lesions.

The war neuroses present another problem of immediate concern to neurologists and psychiatrists, but it is a rather striking fact that to date in England,

even among the civil population, the incidence of neurosis appears to be less than in peace time. There were a few shattered men returning from Dunkirk, who had the characteristic symptoms of "shell shock," such as were encountered in the last war, but these for the most part cleared quickly, and I was told on good authority that others who were slow to throw off the psychological effects of their harrowing experiences were greatly benefited by the administration of testosterone propionate!

The incidence of war neuroses no doubt provides an indication of the morale of a country at war, and their surprisingly low incidence at the present time in England, along with the thousand other signs, indicates that the morale, both in the services and among the civil population, remains exceptionally high.

Weir Mitchell proved that medicine, especially neurology, could be advanced in times of war. He indicated a method which, if followed, will bring information important for the science of medicine, important also for the more successful conduct of war. In our hour of imminent danger may it be possible for us to follow his precepts, and may we all take inspiration from his high example.

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A Health Program for the Homeside in Wartime*

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SINCE the signing of the Selective Service Act, our country has been going forward to the mobilization of its man power for total defense. Never before has the word "total" carried a significance so completely inclusive as it does in this present military effort. Never before has war, and especially its avoidance, demanded the arming of such great numbers of able-bodied men; never before has the equipping of its forces required so much technical skill and so much scientific knowledge; and, never before have the industries been called upon for productions of such magnitude. Never before has the conservation of our man-power for all these necessities compelled attention so specifically and so comprehensively. We are able now as never before to protect our armed forces from the waste that is the result of preventable disease.

And since the Army and Navy are so dependent upon the uninterrupted capacity production of our factories, we are equally cognizant of the need for disease prevention and health promotion among industrial workers.

Persons concerned with research and administrative activities aimed toward improvement in the public health have accumulated a body of knowledge which they have hoped might sometime be applied totally in practice. The time has come when we are to approach a realization of these hopes. Our armed forces will be selected carefully, and there will be a minimal number of mental and physical defectives among them; after their enrollment and equipment, these healthy men will be protected against disease by every known practical measure.

Our industrial workers will receive the same type of care and protection. Plans for the necessary administrative procedures which will accomplish such results are already formulated and are being put into practice.

Then what of the home side? There are as many reasons why our civil population should be protected from the ravages of preventable disease as there are for the guarding of factory employees and soldiers and sailors against accidents and infections. If there is a difference, it resides merely in the difference between "ought" and "must," or possibly in the speed with which the "must" shall be applied.

With regard to the need for these activities there is no disagreement anywhere. Certainly there is no disagreement among those persons who are in charge of our health departments and health boards. They know what to do, and they want the opportunity to apply the knowledge they possess. With the efforts now being made in behalf of our armed forces and the workers in our

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mobilization industries, it is timely to review some of the things that our health departments would like to do, the techniques by which they would do them, and to discuss reasons why such measures should be put into practice.

HEALTH AND EFFICIENCY

National strength that is realistic and enduring can develop to its full potentialities only as an outgrowth from a physically and mentally vigorous citizenship. Health has always been a human value that people have made strenuous efforts and great sacrifices to regain, but a concept of the systematic prevention of disease by scientific procedures is a fairly recent development in the long sweep of history. It is strikingly true, however, that if there is *any* good that comes out of the fear of conflict, it is the acceleration of the application of known, thoroughly tried measures to promote public health, as well as sometimes a stimulus which produces new knowledge. In former days, this speeding-up has applied largely to the mobilized portion of the populace, but now when we are forced to think and to plan in terms of total defense because of the threat of total war (which man's scientific ingenuity has made possible), the job of producing fighting strength for self-preservation involves every man, woman, and child quite as definitely and seriously as it does enlisted men.

The means for the promotion of physical and mental health and efficiency are no different in times of stress from those that we know should be used routinely. However, action which has long been clearly indicated by the facts available to physicians and to public health officials—and to a rapidly increasing extent to the general public—becomes not merely desirable, but urgently essential.

There are certain basic, thoroughly tried public health services which must be provided routinely and efficiently through organized community effort, even before it is practicable to undertake the more difficult and expensive measures, which have been developed in many of our progressive communities. We know how to control most of the communicable diseases, but the evidence that we are not applying our knowledge to the best advantage is painfully abundant. For example, we are still burdened to a disgraceful extent with acute communicable diseases like scarlet fever—and even diphtheria and typhoid—which can be prevented by comparatively simple measures. The fact that hospital beds and the skill of physicians and nurses are still required by victims of these—and other—preventable diseases is an indictment of our social and medical organizations.

Scarlet Fever

The evidence favoring mass immunization against scarlet fever is even stronger than it was in the case of diphtheria 40 years ago, yet there remains a certain resistance to the new—and not so *very* new, at that—which we must always expect, but which, when prolonged past the point of newness, is unbecoming in men with the background of a medical education. The experience of the physicians of the Department of Public Health of Philadelphia, as reported by Dr. Harriet L. Hartley,[1] indicates beyond any question the success with which scarlet fever immunization *can* be administered.

[1] Hartley, Harriet L., The Practical Administration of the Dick Test and Scarlet Fever Toxin Treatment, Hahnemannian Monthly, LXXIV (9): 724–732, (Sept.) 1939.

However, we continue to spend many thousands of dollars more on the treatment of scarlet fever than would be required to Dick test every child and to immunize the susceptibles. In Philadelphia during the last 15 years, we have had over 60,000 cases of scarlet fever *reported* (and we doubt that the reporting is complete). Some 40,000 of these have been treated in our Municipal Hospital for Contagious Diseases. This number gives us an average of roughly 4,000 cases a year (although there has been much fluctuation in the yearly incidence), with between 2,500 and 3,000 being hospitalized annually at public expense. The per diem cost to the City is about $4.00, and the average number of hospital days per patient is 30. In other words, it costs the City about $120.00 to care for *one* case of scarlet fever, and to care for 3,000 cases the taxpayers must furnish $360,000. This figure does not include the expense to families prior to admission of their sick children to the hospital, and it does not include the money that is needlessly spent by those families in which the cases are treated at home and not hospitalized by the City.

Suppose we should consider immunizing all children in Philadelphia under 15 years of age. There were less than 500,000 in this group in 1930; the 1940 census will probably show an even smaller number. According to Dr. Hartley, the actual cost of materials, for the Dick test and five immunizing doses of toxin, is $0.65. Many Philadelphia children have already been immunized; many of those who have received no injections are immune, but even if every one of the assumed 500,000 children had to receive the complete treatment, the bill for materials would be only $325,000.

Then, subsequent to this hypothetical year of mass immunization, the annual cost for keeping the non-immunes immunized would be small, since we have fewer than 30,000 live births a year. (Note: In 1937, there were 28,492 babies born to Philadelphia residents.) Assuming that every baby at 18 months old was found to be susceptible to scarlet fever, it would cost less than $20,000, for materials alone, to protect them all. The annual expenditure of so small a sum, relatively speaking, would leave us a balance of $340,000 which we now expend as a result of our professional failures. That amount of money could be invested in health procedures which would pay larger dividends than the treatment of preventable cases of scarlet fever does.

The argument is all too often advanced that since the incidence of scarlet fever is so low, immunization is not necessary. The fact that 1,897 cases were cared for in the Hospital for Contagious Diseases during the first 8 months of 1940 does not seem like a low incidence to me, but if it does to some, let us consider the incidence of diphtheria. Nobody would think of protesting against diphtheria immunization. Yet we had *75 times* as many cases of scarlet fever hospitalized at public expense during the first 8 months of 1940 as we had diphtheria cases. (Note: scarlet fever, 1,897 cases; diphtheria, 25 cases.) If it is a matter of the fatality rate which the skeptics question, we have the hospital record of 6 deaths during this period from scarlet fever and none from diphtheria.

Another argument which is sometimes proposed against scarlet fever immunization is that the reactions are worse than the disease. We had the same emotional objection, of course, back in the 19th century against small-pox vaccination. The only possible excuse for

such an attitude is that the observations have been of too few cases, and those probably before the introduction of the improved technique and toxin now used. Dr. Hartley found in her analysis of 1,600 cases treated with scarlet fever toxin that 4 out of 5 had *no* general reactions, and that less than 1 per cent (actually 0.2%) had severe reactions (fever to 103°, vomiting, and—very occasionally— a rash). Even these rare cases in which the reaction is severe do not compare with the sequelae and danger of death that accompany the disease. There has never been a fatal reaction. Immunization leaves no mastoid infections, cervical adenitis, arthritis, nor kidney and heart disease, which scarlet fever may leave even with the best of care.

In the experience of Dr. Gladys Dick, an experience running up to hundreds of thousands of immunizations, there has never been an attack of scarlet fever in a child negative to the Dick test—that is, naturally immune—or immunized. In the practice of a few physicians there have been attacks of scarlet fever in children who had reacted negatively to the Dick test. When such a thing happens, it is pertinent to question the accuracy of the Dick test that was made. There are sources of error in the making of the test and in reading the results. Inaccuracies are likely to be common unless every detail of the prescribed technique is followed with painstaking care.

Any question concerned with the efficiency of immunization is completely answered by the experience of contagious disease hospitals. Immunization against scarlet fever is routine practice at our Municipal Hospital, as it is in many others. It is the only method known at present by which the exposed doctors and nurses can be insured against infection.

The question of whether the children shall be immunized by their family doctors or in public clinics must not be permitted to hinder the extension of opportunity for immunization to every child at the appropriate age. There has been an unfortunate impression among physicians in some areas that large scale immunization programs, whether for diphtheria, typhoid, or scarlet fever, by health departments, interfere with private practice. Actually, no such thing happens. In those communities where this question has been studied without pre-judgment, and careful records have been kept, it has been found that as immunization increases in the public clinics, the demand for it also increases among patients who consult their family doctors. This initiative taken by patients able to pay was due, of course, to the high educational value of immunization programs.

To return to the hard, material, dollars and cents basis which we must use in view of the economy demanded for building national defense, failure to stamp out scarlet fever entirely tends to negate the sincerity with which we avow our intention to concentrate on national strength.

Typhoid Fever

Although we have progressed so far since the times when we had large epidemics of typhoid fever that civilian health officials no longer consider the infection a major problem, we are reminded all too often by small outbreaks that vigilance is still demanded. Within the last year, two of the students from our Department at the University who have become State District Medical Officers, have, by careful epidemiological

work, ferreted out 25 cases in three counties. There were 3 deaths. Let me remind you that this occurrence was in 1940. Several carriers were concerned—at least one of whom was a food handler—and there appears to be an infected private water supply involved, too. However, the details are not our interest here. The significant facts are that these outbreaks did occur, and that trained workers identified the source in each case and acted accordingly to check further spread. The implication of this and other similar experiences is that the administration of the public health must be in the hands of trained men. The devotee of specious skepticism might say that outbreaks of typhoid fever occur only in those places where the community's health has been intrusted to a well-educated medical director. Evidence to support this is contained in the fact that one of the cases of typhoid fever had been diagnosed pernicious anemia.

Pneumonia

The problem of pneumonia control is another which requires the closest coordination of the work of the Health Department and the private physician. We have in Pennsylvania, as a direct result of the planning of Dr. John J. Shaw, an effective, functioning system for the modern treatment of pneumonia. The quick action necessary for laboratory services in typing the causal organism, and the ready availability of serum which is too expensive for many—perhaps most—patients to buy, offers strong evidence of the need for closer and more extensive coördination of public health services with the work of private physicians. The success which our State has had, and will have, in reducing the fatality of pneumonia, will rest largely on the diligence we use in teaching people to call the doctor early, so that a diagnosis may be made soon enough to apply the serum and chemotherapy which have proved so effective. The laboratory facilities for typing, and the therapeutic sera for treatment have been made available by the State.

Tuberculosis

The control of tuberculosis and syphilis is even more tedious and expensive than the prevention and treatment of acute infections, but that fact in no way diminishes the intelligent hope to which we are entitled, that they can and will be eradicated. Tuberculosis has declined so rapidly that we may be inclined to think it will go on declining by itself. But the fact that it is not declining as rapidly now as it did in earlier years bids us take care.

The discovery of tuberculosis requires great skill and careful planning, but the rewards in terms of early, curable cases far more than justify the expense and effort. The release of energies we are forced to spend on the care of the victims of tuberculosis, and for the support of their dependents—all this, apart from the human happiness or misery that is at stake—would make way for much public health work that is on the positive side rather than the negative. We had 4,195 deaths from tuberculosis in Pennsylvania last year. The fact that tuberculosis tends to increase dramatically in wartimes, sometimes even in non-belligerent countries, renders the work of controlling this expensive disease even more pressing right now.

The Canadian experience in handling the tuberculosis problem during recruiting is valuable for us. Dr. J. D. Adam-

son,[2] Professor of Medicine at the University of Manitoba, says that the standards which prevailed in the Army for examining recruits during the first world war did not yield satisfactory results, and have been modified accordingly. He summarized the magnitude of the tuberculosis problem in Canada, during and after the last world war, thus: "For every 100 killed in action, six have died of tuberculosis; for each 100 pensioned for wounds, 25 have been pensioned for tuberculosis. . . . The important fact is that no special measures were taken against tuberculosis and, as a consequence, there was much preventable disability and deaths charged against the state. It has been estimated that the bill has been 150 millions."

Dr. Adamson states that "The reasonable aim of all tuberculosis workers is complete eradication of the disease. . . . Conditions of individual control and supervision in the army are such that it should be a fairly simple problem. An effort in this direction is imperative for humanitation reasons and also to improve the efficiency of the army and to reduce the post-war pensions obligations.

"At the beginning of this war, the Defense Department of the Dominion set out to accomplish this end. They realized that tuberculosis can be found best by X-ray and therefore have ordered a chest plate of every recruit. . . .

"As a result of this practice, it can be said that the Canadian Army is free of tuberculosis that is significant, either as a source of infection or a potential cause of disability."

It is interesting to note that a prediction was made of the number of cases of significant disease that would be found among the Canadian recruits. The results of the examinations found that prediction to be accurate. The figure predicted was 20 times the death rate. Significant disease was defined as including not only those cases which were active, but also those in which the lesions were of wide extent or apparently unstable. It is usually assumed that there are at least five times as many active cases living in a community as there are deaths. Dr. Henry D. Chadwick, former president of the National Tuberculosis Association, estimates that there are 10 active cases for every death, and that four of these need institutional care. The conservative figure of five active cases used in the Canadian prediction will vary considerably in proportion to the diligence with which accurate reporting and case-finding are conducted. In some areas the proportionate number of unknown cases is much larger. In the age group between 21 and 35, the incidence would be about twice as high as for all ages. In Philadelphia last year, the death rate was 63 per 100,000. Using the same cautious procedure that Dr. Adamson used in making his prediction, we would expect in Philadelphia to have about 1,250 rejected men out of every 100,000 recruits because of tuberculous infection. The Canadian figure of 1,000 out of every 100,000 would be perhaps a little higher than we may expect to find for the United States as a whole, but not much. Dr. Adamson's general conclusion is that 20 recruits will be discarded for every one of the population that dies each year of tuberculosis.

If the same careful examinations are made in the United States as are being

[2] Adamson, J. D., Canada Eliminates TB from Army, Bulletin of the National Tuberculosis Association, **26** (11): 163–4; 171, (Nov.) 1940.

made in Canada—and we know that they will be—we are going to have a wealth of information available as well as an abruptly increased load of patients to be cared for. Under existing law, manifest or suspected cases of tuberculosis must be reported immediately to the public health officials. The impetus that the Army case-finding work will give to case-finding among the civilian population will be of untold value in taking a step in seven-league boots toward our goal of eradication. Not only will the advantage of early knowledge of his disease and prompt treatment be given to the unfortunate draftee who is infected—for which care and treatment the community, not the Army is responsible—but also the opportunity must be given to the intimate family associates for thorough examinations and prompt treatment if it is found to be indicated. Discovery of new cases and bringing them under control at this time will go a long way toward making the homeside healthier and stronger and more able to give of its strength to the common good of national defense.

Many of the rejected men will be under the care of their family doctors. Upon these physicians will rest a great deal of the responsibility for consolidating the ground gained for us by the new information presented by the Army examinations. Among the young men who are called up, there will be found individuals in every stage of tuberculous infection. Some of them will be in so advanced a stage that they will need immediate hospitalization. We know that our State Department of Health is making efforts to provide clinics for the treatment of ambulatory patients and hospital beds for those patients who require them. General Reynolds tells us we are still short of Dr. Chadwick's figure of four beds for every death, but that when work now under construction is completed, we shall have sufficient beds in Pennsylvania to accommodate the 600 to 700 persons awaiting admission. We shall have a little better than two beds per death. But what will happen to that waiting list when many new cases are revealed by the findings of the Army examinations? If it goes up, the communities must stand prepared to build more hospitals and offer more clinic facilities for the care of the tuberculous. With the times of stress which are surely ahead, honest desire to improve the health of the homeside in wartime leaves no choice to the citizenship, but to make it possible for our State Health Department to provide the facilities and medical care that will be needed. It will cost money, but it will save many times what it will cost.

Doubtless many of those identified by the X-ray as early cases can be successfully treated in their homes. With adequate care a certain proportion of such men can overcome their disease in their homes if they receive skillful treatment. We have a comparable experience in the work of the Student Health Service at the University of Pennsylvania. Dr. H. D. Lees, by use of the tuberculin test, X-ray, and careful physical examinations, discovers a number of such minimal cases every year. In the past five years, a great many infected students have returned to their classes in from six months to a year. The experience of Dr. Lees is illustrative; it is by no means unique. Any physician can do such a job equally well provided he sees to it that his knowledge of the technique of care and treatment is on a level with that of Dr. Lees.

The family physician will be responsible not only for the supervision of pa-

tients discovered by the Army's X-ray program, but upon him will rest, along with the Health Department, the job of locating and examining the contacts of these men. The search for the source of their infection and also for the secondary cases that have developed from the open cases that are sure to be found must be a relentless one. The family doctor must know and use the same high type of examination that has been proved to be the only way tuberculosis can be found in its early stages. That means X-ray of the chest plus the usual physical examination. The stethoscope is an obsolete instrument for discovering early tuberculosis. It will sometimes miss far advanced cases even when used by the most skilled diagnostician.

Syphilis

Another chronic disease of which many new cases will be found in the examinations of drafted men is syphilis. The rapid strides that have been made in the last few years in its control are encouraging. The same responsibility for the treatment of rejected men will exist. Physicians in private practice and public health clinics must treat these cases, and discover the sources and secondary infections. Greater demands will certainly be made on the laboratories, epidemiologists, and public health nurses, as well as on the physicians in private practice. Accompanying the increase in work to be done is a vast opportunity to decrease the incidence of syphilis in the civilian population.

Another phase of the problem of health protection of the homeside in wartime is the control of venereal diseases in areas where armed forces or national defense employees are concentrated. Already an agreement on policy has been reached by the War and Navy Departments, the Federal Security Agency, and State Health Departments.[3] The diagnosis and treatment of enlisted personnel infected with the venereal diseases is, of course, the responsibility of the Army and Navy, but the community, through its organized public health activities, is equally responsible for the diagnosis and treatment of the civilian population. The control of sources of infection is one of the best services the public health authorities can render to the health protection of enlisted men. The policy that has been agreed upon is as follows:

"All contacts of enlisted men with infected civilians to be reported to the medical officers in charge of the Army and Navy by the local or State health authorities.

"Recalcitrant infected persons with communicable syphilis or gonorrhea to be forcibly isolated during the period of communicability; in civilian populations, it is the duty of the local health authorities to obtain the assistance of the local police authorities in enforcing such isolation.

"Decrease as far as possible the opportunities for contacts with infected persons. The local police department is responsible for the repression of commercialized and clandestine prostitution. The local health departments, the State Health Department, the Public Health Service, the Army, and the Navy will cooperate with the local police authorities in repressing prostitution.

"An aggressive program of education both among enlisted personnel and the civilian population regarding the dangers of the venereal diseases, the methods for preventing these infections, and the steps

[3] Control of Venereal Diseases in Areas Where Armed Forces or National Defense Employees are Concentrated. Venereal Disease Information, **21** (9): 277, (Sept.) 1940. U. S. P. H. S.

which should be taken if a person suspects that he is infected.

"The local police and health authorities, the State Department of Health, the Public Health Service, the Army, and the Navy desire the assistance of representatives of the American Social Hygiene Association or affiliated social hygiene societies or other voluntary welfare organizations or groups in developing and stimulating public support for the above measures."

The quality and quantity of the control work agreed upon for handling venereal disease in the extra-cantonment zones is limited by the support which it receives from the community. The most effective educational work will be that done by physicians and nurses in their direct working relations with patients and contacts. There is need, also, however, for skillful interpretation of venereal disease control measures to taxpayers. Although every physician and public health worker must do some educational work if his own efforts are to be utilized fully by the community, it has become clear that public health education is a specialty and requires trained personnel for its execution. The purposefulness of health education is made more precise by the impetus given it by the increased need for building national strength. Dr. Thomas Parran had the insight and courage to point the way in 1937 and to keep on giving his assistance in informing the people of the dangers of syphilis and, more importantly perhaps, in developing procedures for making prompt and thorough treatment available in an acceptable manner to every infected individual.

Even if our civil communities fail to take advantage of every other opportunity to control disease, which will be offered them by this mobilization, their thorough coöperation in the venereal disease program alone will bring returns reminiscent of the Spanish-American War and yellow fever.

Air-Borne Infections

Among the problems that always accompany war is the threat of epidemics. No horrors of sudden and violent death which are associated with actual combat during the first World War can compare with the devastation wrought by influenza. Already we hear rumors of increases in respiratory infections, which are bound to occur under the abnormal conditions to which the peoples across the seas are subjected. We are blessed with a means now which we did not have in 1918, for combatting the spread of crowd diseases. The studies of William Firth Wells on the bactericidal irradiation of air have shown that the epidemic spread of childhood infections in schools can be prevented. He has found that ultra-violet radiation that is adequately applied will destroy streptococci, the virus of influenza, tubercle bacilli, and many other organisms which have been expelled into the air. This work has progressed far enough to warrant the large scale installation *and expert supervision* of ultra-violet radiation, not only in the barracks, mess halls, and hospitals where recruits will be confined, but also in all those places where large numbers of civilians will be gathered. Ultra-violet lights, which have proved to be protective in hospital wards and schools, will be the factor which, if utilized intelligently, will tend to check the epidemic spread of respiratory diseases which have been so devastating, not only among our enlisted men, but also among our civilian populations in past wars.

Maternal and Child Hygiene

The declining birth rate during recent years has resulted in a shift in the proportion of young people in the population as a whole. Fortunately this decline in the birth rate has been co-incident with a sharp decline in the neonatal, infant, and maternal mortality rates. The evidence is strong that the greater protection for babies has been the result of concerted public health work in the field of maternal and child care as well as from the admirable improvement in the knowledge and skill of physicians. Although we in America are not concerning ourselves with the policy of attempting to increase our numbers of well-born and carefully nurtured babies for the deliberate purpose of increasing our fighting strength, we do know that the hazards which mothers and babies must undergo are also increased when the resources of the country are being mobilized for wartime needs. It is not that we must refrain from neglecting maternal and child care as our attention is brought into sharper focus on the problems of industrial and military speed-up, but rather that the gaps in our present methods must be closed. Our program must be expanded until preventable causes for maternal deaths no longer exist and until every baby is well-fed, well-housed, appropriately immunized, and taught the habits of life that lead to emotional and physical health as he grows into adulthood. This phase of a public health program is the very foundation stone on which the strength of the nation rests.

Dental Hygiene

Closely allied to the protection of mothers and babies is preventive and educational work in dental hygiene for growing children and adults. Our lack of knowledge of the cause of dental caries leaves us with but one procedure. It is expensive, but it is an essential one. The opportunity must be made available for every school child to have his teeth examined and cavities filled at regular intervals. The advantages of such a procedure would be twofold: first, checking the destruction of teeth while the cavities are small, and, second, the formation of the habit of regular dental care. Although teaching a child to brush his teeth and to eat balanced meals is an entirely laudable procedure, the most important knowledge we have to offer anybody about saving his teeth is that it is essential for him to go to his dentist regularly for cleaning, examination, and reparative work. It is true that many children and adults, too, fail to obtain dental work early for financial reasons; it is also true that many neglect such work through lethargy. The gravity of this problem could not be better revealed than by the large numbers of men who were rejected in 1917 because of carious teeth. We have had surveys and surveys of dental needs. We need no more. We *do* need the wisdom and energy to develop a system that will result in regular and efficient dental care for the entire population.

The magnitude of this problem has been studied by Klein and Palmer,[4] of the U. S. Public Health Service. They found that the yearly increment of carious lesions arising in the permanent teeth surfaces of elementary school children is approximately 1.3 per child. Provision must soon be made to have this much reparative work done. The expense will be borne privately and publicly—the

[4] Klein, Henry, and Palmer, C. E.: The Dental Problem of Elementary School Children. The Millbank Memorial Fund Quarterly, **16**: 267–286, July, 1938.

apportionment of financial responsibility must be worked out by each community. It is predicted that the dental profession will soon find a way to get this done.

Public health in England got its start when the children employed in newly developing industries began to die off like flies. Employers, fearing the supply of child labor might run out, began to wonder if more sleep in somewhat ventilated and reasonably clean and not quite so crowded quarters, only twelve hours of work, or so, a day (except, of course, in rush seasons) and a little more food might reduce the labor turn-over. The big water-borne epidemics of cholera and typhoid fever had produced so much distress that big steps in engineering to prevent explosive outbreaks were already being taken. Sometime later John Snow[5] studied the Broad Street pump and later William Budd had some thoughts about typhoid fever and soon the bacteriological era was under way.

RELATION BETWEEN THE PRACTICING PHYSICIAN AND THE PUBLIC HEALTH DEPARTMENT

Our medical profession's intimate knowledge of the suffering and loss of energy and time which are produced by preventable sickness was one of the major factors that brought about the organization of community efforts which have crystallized in public health departments. It is chiefly the result of their efforts that we have a system of reporting births, deaths, and communicable diseases which enables us to take an inventory of our problems. William Farr and J. S. Billings showed us the advantages of reporting and carefully appraising health conditions by the statistical method. Here again we find the public health dependent in a large way upon the adequacy with which physicians report to a central office the details of vital statistics in order that meaningful patterns may be discerned in them. Knowledge of epidemiological sequences may make all the difference in the rapid checking of an explosive outbreak of contagions.

We have already mentioned the im-

[5] I have often wondered about John Snow and the arguments he must have had with the old gaffers who stood about and told him they had always used Broad Street pump water and their fathers and grandfathers had used it before them. They had all found it entirely safe. Did they look as though they were dying of cholera? They needed no upstarts to tell them their well was polluted and its water dangerous. If you will select the proper night when the moon is waning and will go quietly up the East River Drive you will find reincarnations of all those old gaffers huddled about the heavily polluted springs there, quaffing draft after draft of that—not too—diluted sewage and telling one another that Hubley Owen [Director of the Department of Public Health of Philadelphia—*Ed.*] is just about as dumb as John Snow was. By day these reincarnated old gaffers subsist on raw milk. The administrative skill which Dr. Herman Biggs used in checking the threatening spread of cholera in New York during the nineties was an important factor in the development of confidence on the part of the people in its health department. We have come to consider a safe water supply and an adequate system of sewage disposal as necessities which must be routinely provided. There are other phases of environmental sanitation which are not so clearly accepted. We in Philadelphia may at last congratulate ourselves that we are on the way, however belatedly, to having raw milk excluded from our City's supply (as of January 1, 1941). We do not want our people exposed to the risk of even raw Certified milk. Even with the most rigid precautions and frequent inspections no raw milk can ever be completely and invariably safe; as properly pasteurized milk, properly handled, *is* invariably safe. The constant and thorough supervision of pasteurizing plants is, of course, taken for granted as essential. In the phosphatase test we have a new and reliable safeguard. The popular milk of the future will be homogenized. It seems to have everything in its favor.

munization programs which have grown up as a result of the demands of physicians who have seen misery and death which is beyond their powers to control but which could be prevented. Tuberculosis and syphilis clinics have developed because physicians saw the necessity for them. The job of expensive and time-consuming diagnostic procedures and treatment on a large scale is beyond the capacities of even the most generous of altruistic physicians. Public health laboratory services, too, have reached their present capacities and are being expanded because physicians in private practice have demanded them. These laboratories are continuing to increase the scope of their activities to meet the demands made by the greater precision with which modern medicine is practiced. Mention has already been made of this situation in the case of pneumococcus typing.

The releasing of private physicians from the burdens they often assume for indigent patients should be furthered by the extension and maintenance of prenatal, well-baby, and pre-school clinics. It is probably true that no sick baby is ever refused care, but the regular preventive work which keeps babies well certainly does go undone when there are no well-organized services available to supply them. The availability of such services as those rendered by the Children's Hospital and the Babies' Hospital of this city is a boon to the busy physician who needs help in the cases of patients unable to pay.

In addition to the control of communicable diseases, the collection and analysis of vital statistics, laboratory services, maternal and child hygiene, environmental sanitation, and public health education, which, as we have seen, must beyond any doubt be supplied and expanded for the entire civilian population, there are other public health services which should be developed after the basic ones listed above are established and functioning efficiently. The emphasis and rate of development of each of these varies with local needs.

The problems of industrial hygiene and industrial medicine will be greatly magnified due to the acceleration of armament manufactures as well as of other products which the increasing activity in production indicates. Not that the problem of protecting workers is one applying to factories alone. The communities in which the men and women and their families live must be conducive to efficiency and constantly maintained health. In many instances special precautions will be necessary where large movements of population will occur. With adequate precautions ahead of time, the difficulties that are known to be probable may be obviated.

As noted above, coöperative work has been organized which will leave nothing to chance in the matter of the conservation of our man power in industry. We shall hear more of this work. For us it serves to emphasize our responsibility to the homeside people. Work for their health and well being cannot be permitted to lag behind that being done for that moiety of our population which is directly concerned now with mobilization.

NUTRITION

The epidemiology of dietary diseases has not been long considered as a "must" among the medical health officer's charges. It is true that this matter has been considered incidental to the problem of dental caries, antepartum care, and in well-bay clinics. Probably there is no preventive force in a community

health program of any greater potential worth than sound nutrition work. It is true that our public health nurses accomplish a great deal in teaching homemakers the principles of nutrition, but the problem is a bigger one than individual nurses can handle. Eventually, the community must protect the health of its citizens by being sure that protective and nourishing foods are available at all times in its markets at a price people can pay. We know all too well that an undernourished population furnishes a fertile field for the tragic breakdown of health on a large scale. Nutrition studies and recommendations for large groups is work which demands specialists. The time will doubtless come when we have experts available who will be responsible for appraising local problems of malnutrition and determining the appropriate means of solving them. Much can be accomplished by coördination of efforts that are already being made.

MENTAL HYGIENE

It is probable that the handicap which leads to more inefficiency than all the diseases and physical defects combined is due to emotional maladjustment. It seems reasonable to guess that the extent of such disorders will not decrease with the social changes which will occur as the demands on our energies increase and our capacities for altering our ways are taxed.

We have no large-scale index to the extent to which mental disorders and diseases prevail in any community. We do know that there are more beds in hospitals registered with the American Medical Association for the mentally ill than for the victims of all other diseases and disorders combined,[6] and that many more beds are needed. However, the problem of institutional care is not so much the issue in meeting the immediate needs for increasing the vigor and stamina of the homeside in wartime. It is combatting those forces which attack the resilience of reasonably stable and well-balanced people toward which our efforts need to be redoubled now.

We know that the ground is prepared all too often during childhood for the development of personality disorders which result in misery and inefficiency. Some splendid steps are being taken to combat this evil by the recognition of its seriousness by workers in pre-school clinics, by public-school teachers and administrators, and in the splendid Child Guidance Clinics which are growing slowly but sturdily. There are so many variable factors involved in the mental hygiene field that it is beyond the scope of this discussion, but its importance and wide implications warn us that every means of eliminating the causes of maladjustment must be used. The problems of convalescent care, the rehabilitation of those persons who are recovering from chronic illnesses, the school health program, recreation facilities, low-rent housing, maternal and child welfare, as well as many others, are all related in varying degrees of directness to the prevention of mental disorders.

A first step can be taken, if a community is determined to prevent mental disorders, by ascertaining the size and scope of the problem.[7] Then a second can be made by comparing the available facilities for handling it with acceptable standards elsewhere. That second step is not easy, because mental hygiene is in a developmental state, and there is not agreement on absolute standards. How-

[6] Hospital Service in the U. S. J. A. M. A., **114** (13): 1166–1167, 1940.

[7] Hiscock, Ira V.: Community Health Organization, Commonwealth Fund, 1939, pp. 213–222.

ever, the value of guidance from psychiatrists and psychiatric social workers during the early stages of the development of abnormal tendencies has been proved beyond question.

Heavy burdens can be removed from the potentially fit by the provision of insitutions for the care of the temporarily or permanently unfit who require them, either because of illness or defectiveness. The advantage of institutionalizing those mentally ill or defective persons who need it is twofold: first, they have a better opportunity to become capable of being productive and independent; and second, their families and friends are relieved of the burden of fruitless efforts in their behalf. In some instances, proper institutionalizing may preclude the probability of destructive behavior which is costly, as well as damaging in other ways, to the community.

For the large number of patients or potential patients who do not require institutional care, some health departments have provided out-patient clinics, some of them permanently located and some traveling on a regular schedule so that the skill of experts may be available even in smaller communities. The public health nurse is a key person for the success of such a plan.

Problems of defense do not create new needs in the field of health protection, but they do emphasize the importance of increased efforts toward extending public health activities. The principles of public health administration are the same now as they were a year ago, but the powerful forces which drive us to arm in a military way also force us to build the health of the citizenship upon whom so much depends in modern defense.

John Jones' Introductory Lecture to His Course in Surgery (1769), King's College, Printed from the Author's Manuscript

With an Outline of the Succeeding Lectures and of His Notes on the Lectures of William Hewson

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INTRODUCTION

EXTANT examples of the earlier lectures delivered in the first two medical schools in the Colonies are extremely rare. The probability is, that the system of providing students with syllabuses was not imported until the schools had become fairly well established. Thus, while students' notes on the lectures of their professors from the 'eighties on are progressively more available, those that have survived from the first decade of the medical schools are few indeed. As the didactic lecture, read from manuscript, was the customary method of teaching, it might be supposed that a goodly number of the professors' own manuscripts would still exist; but such, unfortunately, is not the case—unless they have not yet found their proper way into our medical libraries. In other words, we have very little of primary source material on the beginnings of organized medical teaching in this country.

John Jones (1729–1791; the most famous surgeon of his day in the Colonies), when, in 1767, he was elected professor of surgery in the medical school of King's College, in New York City, then in process of being organized, became the second professor of surgery in this country.[1] In 1775, as is well known, he published a manual of military surgery, our first native surgical text-book.[2] A third edition appeared in 1795, brought out by Jones' friend Dr. James Mease, of Philadelphia, who added a biography of the author, Jones' "Case of Anthrax" (originally published, 1793, in vol. 1, pt. 1, of the *Transactions* of this College), and an "Uncommon Case of Hydrocele," which Mease says he came upon while "perusing the manuscript lectures of my deceased friend." This little volume of "Surgical Works of the late John Jones, M.D." has been until now our major source in any study of the life and works of this distinguished American surgeon.

The manuscript volume[3] which it is

[1] William Shippen, in Philadelphia, was, of course, the first (1765). No examples of Shippen's earlier lectures survive, to the best of my knowledge.

[2] "Plain concise practical remarks on the treatment of wounds and fractures," etc. New York, 1775.

[3] The ms was given to the library in 1902 by George W. Norris, M.D., to whom it was presented, a penciled note states, "by Mrs. Randolph." On a fly-leaf, in ink and in the manner of a title-page, is written: "Lectures on Surgery by the late John Jones, M.D. presented to me by Mrs. Clark." This seems to be in the hand-writing of Dr. James Mease, whose signature appears in the upper right-hand corner. As has been said above, Dr. Mease

our privilege here to bring to notice has the potentiality of adding appreciably to our knowledge of the earliest medical-school teaching in the Colonies and of the most highly esteemed of our early surgeons. The Introductory Lecture, printed here for the first time, may be regarded as a companion piece to Peter Middleton's "Medical Discourse, or an Historical Inquiry into the Ancient and Present State of Medicine," delivered at the opening of the medical school of King's College and printed in 1769; and to Samuel Bard's First Commencement address, printed in the same year. The brief outline of the succeeding lectures and of the notes on William Hewson's lectures it is hoped may stimulate other hands to investigate further a capital bit of original source material.

It will be remembered that in 1780 Jones moved to Philadelphia, where his fame and influence continued to grow, though the presence of Shippen on the medical faculty here naturally precluded any professorial appointment. In 1786, Jones participated in the founding of the College of Physicians of Philadelphia and was elected its first vice-president, an office which he held until his death in 1791, when, curiously enough, he was succeeded by Shippen. Thus, though the manuscript in our possession was written at the other end of the Philadelphia-New York medical axis, this publication by the College of Physicians of Philadelphia has a certain logic and appropriateness.

Introductory Lecture[4]

By John Jones, M.D.

(1) The advantages attending the establishment of a medical school, in this city, as well as the History of Physic in general, have been so fully explain'd by Doctor Middleton, & the other gentlemen Professors, in their learn'd introductory Lectures, that very little can be added to those subjects. for which reason I shall confine myself, particularly, to that branch of medicine, to which I have the honor to be appointed a Professor, by the respectable governours of this colledge, to whose public spirited views the present infant attempt, to found a regular medical school, owes its first encouragement.

and though this public testimony, of the favourable opinion which the governours are pleas'd to entertain of my abilities, forbids me to think myself

brought out, in 1795, a third edition of Jones' chief publications, adding to them a description of an uncommon case of hydrocele which he found in the manuscript lectures of his friend. The description appears in our ms substantially as it reads in print; for this reason, as well as other, obvious ones, it seems unquestionable that this was the ms Dr. Mease was "perusing" when he came across the case.

[4] Transcribed literally. Peculiarities to be noted are: the double 'e' in the word 'we'; the transposition of the vowels in the diphthong 'ie'; inconsistency in the use of an apostrophe in place of the letter 'e' (e.g., *confin'd*), and in the use of the letter 'u' in such words as 'labor'; the excessive use of commas; the general disregard of capitals at the beginning of sentences; the misspelling of such familiar words as 'inflammation,' 'mere,' 'scirrhous,' etc.

There seem to be two introductions and two conclusions; the first introduction and the first conclusion I have designated by the number '1' in parentheses; the second introduction and second conclusion, by the number '2' in parentheses; line spaces indicate the divisions between the parts. Where the author has crossed out words and substituted others for them, I have given only the substitutions.

totally unequal to the labour assigned me, yet when I reflect how often I am unable to satisfy myself, in my own private enquiries after truth, it is with the utmost diffidence I enter upon the difficult task of instructing others . . . a task which nothing woul'd have tempted me to undertake, but a sincere desire to promote, as much as lies in my power, the reputation & interest, of my native country. & to merit in some little degree, by the utmost attention & industry, the favorable sentiments of the governors.

In this introductory lecture, I shall endeavour to give an adequate Idea, of the nature & extent of a science, the most truly useful to mankind.

(2) Two years being now elaps'd since the establishment of a medical school in this colledge, & a regular course of lectures in the various branches of medicine having been read by the different professors[5], the public has been enabled to form some judgement of the merit of the institution . . . for my own part gentlemen truly sensible of my defects, & how unequal I am in ability as well as ill health, to fulfill the important task required of a public teacher, I shou'd have declin'd the honor done me by this appointment, had I not been influenced by a sincere desire to promote as far as lay in my power, an institution so evidently calculated to advance the general good of my country as well as the art of surgery in particular. As the history of Physic in general has been so fully explain'd by Doctor Middleton in his learned introductory Lecture & Dr. Bard in his (annual?) I shall confine myself principally to that branch of medicine to which I have the honor to be appointed a professor, & endeavor to give an adequate Idea of the nature & extent of a science, the most truly useful of any to mankind.

Though it is highly probable, that during the first ages of the world, very few remedies were known for the cure of diseases, yet when wee reflect upon the simplicity, & sobriety of men's lives, not enervated by sloth & luxury; it will appear very reasonable to believe, that few medicines were requir'd. temperance & exercise, procuring a higher degree of health, & longevity, than the utmost Improvements in the science, have been able to do, in the more luxurious days of modern refinement.

But man was no sooner banish'd from the seat of innocence & bliss, than he was subjected to those accidents, which constitute many of the principal objects of Surgery . . . and hence we find, that the first Physicians, of whom we have any clear authentic accounts in history, were cheifly exercis'd in chirurgical operations. . . . Such were Machaon & Podalirius, the two sons of the Deifyd Esculapius, who attended Agamemnon, to the Trojan war. & were employ'd as Homer informs us, in curing the wounds of his unfortunate heroes, by the use of the knife, & the application of medicines.

as to internal diseases; the obscurity of their causes, & the superstition of the

[5] This second introduction furnishes the data which lead us to assign the manuscript to the year 1769. The medical faculty was organized in 1767, and the "two years being now elaps'd" would bring the date normally to 1769. Though the organized teaching was evidently not begun until 1768, the first commencement was held in May, 1769. Jones implies that not more than one regular course of lectures had been read at the time of delivery of this lecture, which suggests the summer or fall of 1769. The reference to Dr. Bard's lecture was added to the manuscript apparently as an afterthought, and probably because Bard's lecture, delivered May 16, 1769, had just come off the press.

times, induced men to attribute them to the anger of the gods. . . . That this was really, the opinion of the ancients, may be seen in many passages, of Homers poems, where he mentions Jupiter as punishing wicked nations, by diseases, as well as wars, famine, & other calamities.

But wounds, fractures, & every species of external injuries, were diseases of too obvious a nature, to pass for miraculous, & the Preists of Esculapius, who were possesed of all the medical knowledge then known, cou'd not cure, even a fractur'd leg or arm, by the interposition of their god.

The cure, of these maladies, was commited to meer mortal men, who cou'd not veil their ignorance, in the obscurity of the cause, or the method of treatment. both which, were too evident to the senses of the spectators, for the operator to conceal his want of skill . . . & hence it became necessary, for a man, to make himself truly Intelligent in his profession, in order to acquire a Just reputation.

This ancient branch of medicine call'd Surgery, according to the strict grammatical meaning of the word, signifies, manual operation . . . but the science & art of surgery, tho: more clear & certain in its objects, than that of Physic; is equally various, extensive & difficult of attainment. and I have ever been of opinion, that young Physicians, might lay the truest foundation for medical knowledge, by an attentive observation of those disorders, which surgery presents to their view. . . . For most of those diseases, which are incident to the viscera, & internal parts, are seen upon the external surface of our bodies, & are obvious to the senses, and the curative indications, as well as methodus medendi, in both have a very close analogy.

This opinion, may very easily be supported, by considering the effets of an inflamation, upon any of the external parts, by which a fever is immediately excited, & the disease is terminated, either by resolution, suppuration, schirrus, or gangrene. and the same disease, happening upon any of the internal parts, is distinguished more, by the difference of its seat, than the nature of its cause, or method of treatment. . . . [For this reason, Surgery, may with great propriety be divided, into medical, & manual. . . . The first, comprehends, an infinite variety of diseases, which require the assistance, of both internal, & external applications . . . the last, is confin'd to those cases, which admit of releif, from the hand alone, or assisted with instruments. Hence it will appear very evident, how necessary it is for the student in surgery to make himself thoroughly acquainted with all those branches of medicine, which are requisite to form, the most accomplished Physician; to which must be superadded some peculiar qualifications, to constitute the surgeon, of real merit, & abilities.

Besides a competent acquaintance with the learn'd languages, which are to lay the foundation, of every other acquisition, he must posses, an accurate knowledge, of the structure of the human body . . . acquir'd, not only by attending anatomical lectures, but by frequently dissecting dead bodies, with his own hands. . . . This practice, can not be too warmly recommended, to the students in surgery . . . 'tis from this source, & a knowledge of Hydraulics, they must derive any adequate notions of the laws of the animal oeconomy, or Physiology. . . . Chymistry, and the materia medica, are very necessary to a right understanding of Pharmacy, or composition. . . . To these shou'd be added, some progress in the mathematics, &

mechanics. which I will venture to assert, may be applied with much more safety & utility, to the science of surgery, than Physic. . . . But there must be a happiness as well as art, to compleat the charectar of the great surgeon.

He ought to have firm steady hands, & be able to use both alike . . . a strong clear sight . . . & above all, a mind, calm & intrepid, yet humane, & compassionate, avoiding every appearance of terror & cruelty to his patients, amidst the most severe operations.][6]

Though surgery is one of those sciences which have been cultivated with the utmost industry, & attention, & its progress, particularly during the present century, has been very rapid, new lights having been thrown upon it, by a variety of different discoveries, yet none but very superficial minds can imagine, that the limits of our present knowlēdge are the limits of the art.

The variety & multiplicity of our diseases, & the absolute impossibility of our being able to discover with certainty, their primary causes, leads us into a vast extensive feild where wee are frequently oblig'd, to strike out into new, & untrodden paths. From this view of the subject, arises a very natural & interesting question. . . .

What method ought surgeons to follow, in order to give the highest degree of perfection to their art? . . .

Is it from that experience which is acquir'd from practice alone, wee are to expect this perfection? . . . if that had been the case, the art, wou'd many ages ago, have been at its height.

But there is another source of improvement, equally essential to the perfecting our art, & perhaps with more difficulty acquir'd, than that wee obtain from practice alone.

I mean experimental Philosophy. It is very easy to demonstrate the necessity, of that valuable information, which wee derive from a well regulated course, of Philosophical experiments. Nature, shews herself, but very imperfectly to the naked eye . . . wee ought then to observe her, with every assistance which wee can draw from the refinements of art, & the experience of ages. . . . A mind of the most exalted powers, is only capable of comprehending the superficial appearrance of objects; & without calling in the assistance of Physical experiments, can never penetrate into their original properties.

Observation, & Physical experiments, which form the only basis of surgery, have then, two different objects.

Observation regards the sensible qualities of bodies, the course of diseases, their Phenomena, with the effects which result from the process of the art. Physical experiments, unravel the structure & uses of the parts; the composition of mix'd bodies, the properties of those fluids which circulate in the vessels, the nature of aliments, & the action of medicines . . . yet, these so necessary helps, do not conduct us seperately, to the hidden truths, which may serve to enrich our art.

Observation improves our experiments, & experiments influence our observations; . . . they mutually assist each other, & are like lights united, for the dissipation of obscurity.

Observation alone, may be very imperfect, & fallacious; & has frequently been the source of error, as well as truth. Opinions entirely opposite, often producing an equal number of facts, in support of their equivocal Judgements. The ancients were perswaded, that taking blood from different veins in the same

[6] This passage in brackets appears practically verbatim in the Introduction to the manual, where other parallelisms of thought may be found, too.

arm, produced very different effects. & two thousand years had elaps'd, before mankind were disabused, from so ridiculous an opinion; founded upon the observation of the greatest masters of the art.

But wee are very apt to fly, from one extreme to another.

When Harvey had discover'd the circulation of the blood, those Physicians, who had been most blindly attach'd to the opinions of the ancients, on a sudden regarded them with the utmost contempt. They no longer acknowledg'd any elective remedies . . . the current of blood which flow'd to all parts, must carry the remedies, equally to act upon all. but more exact observations, have oblig'd the most obstinate minds, to return to the ancient opinions, respecting the effects of certain medicines.

Thus physical experiments which discover'd to us the circulation of the blood, led us into erroneous opinions, which observation alone cou'd correct. Observation not only rectifies Physical experiments, but suggests new ones . . . for example, it taught surgeons that a ligature on the arm, stops the course of the blood in the veins . . . that wee must afterwards loosen it, to facilitate the passage of the blood, thro: the orifice made in bleeding. But the cause of this Phenomenon remain'd a secret, 'till the discovery of the circulation . . . (this discovery threw a light upon the observation which was the origin of it.) Thus surgeons who aim at perfection in their art, must sometimes depart from observation, & return to it again, to confirm the conclusions which they draw from Physical experiments.

This course wou'd not be very difficult, if wee had only a few observations & experiments to make, but at our first setting out, difficulties present themselves from all parts. To obtain a knowledge of the most simple truths, requires a long train of observations & experiments which only serve to extend our views, & shew us the necessity of continually repeating our experiments, & observations, in order to make any true progress in knowledge.

The truth of this reasoning will be more clearly illustrated by example.

Blows on the head have frequently occasion'd death . . . the first step which the observation of such accidents requir'd, was to seek out the cause from anatomical inspection . . . opening dead bodies, discovered it to be oweing to an extravasation of blood within the cranium, & evidently pointed out the necessity of perforating the skull, to discharge the extravasated fluid. but further observations, & inquiries, have inform'd us that cases, & those very fatal ones have occur'd, where there is no extravasation; & where the application of the trepan, is entirely useless. . . .

Such are the difficulties which arise in the progress of an art, which requires the work of ages to perfect.

For this reason it becomes necessary to collect the observations, of our predecessors & contemporaries; without whose assistance, the greatest genius, wou'd be nothing more, than an ignorant, & presumptuous practitioner.

Continual study therefore, is equally necessary to the surgeon, as it is to the Anatomist & Physician, who in neglecting to inform themselves, of the new discoveries made in different parts of the world, will become only servile imitators. & perhaps after twenty years labour, be little wiser than their first masters. If the science of surgery requires so much pains & labour, how unjust & inadequate must the Ideas of those people be, who wou'd reduce it to the art of operating

alone. This art, is without doubt very essential to it, & it is operation which principally characterises surgery . . . but the art of operating, consider'd in itself, depends cheifly upon anatomical knowledge, & address of the hands, . . . practice indeed gives this address, in a great measure, but it does not bestow genius, nor the lights which are necessary to conduct it.

Those therefore who estimate surgery by operation alone, & beleive that nothing but long habit & practice, is necessary to form the great surgeon, are grossly ignorant of the art; & those surgeons who found their only merit upon this experience, degrade themselves & their profession; the greatest operators having always been remarkable for the extent of their knowledge, & a contempt for the servile routine of those mean practitioners, whose experience is of little more, than heaping one blunder upon another.

This will more evidently appear from some examples. . . . before the discovery of making a ligature upon the blood vessels, after amputation, the only method of stopping the Haemorrhage was the cruel one of the actual cautery, or red hot iron. a method as terrifying, as it was painful to the unhappy patient. yet near a century elapsed, before the surgeons, habitually bigotted to their old forms, wou'd adopt a more mild & gentle method, the offspring of a happy inventive genius.[7]

The ancient surgeons, & particularly Celsus, boldly, & successfully perform'd the operation, for the Fistula in ano, yet to the shame & reproach of modern operators, there was no one found to undertake it, in the latter end of the last century. 'till the danger to which the life of Lewis the fourteenth was expos'd, by that disease, excited the industry & genius of Falix[8], his first surgeon, who after several experiments upon patients in Hospitals, perform'd the operation with success upon the King, & was rewarded for his services, with a munificence becoming a great Prince.

Thus men of more enlighten'd genius, & more intrepid spirit, must compose themselves to the risque of public censure, & the contempt of their jealous contemporaries, in order to lead ignorant, & prejudic'd minds, into more happy & successful methods.

How much have wee to apprehend from that servile road of imitation which is the sole guide to some men. since it is very certain, that a great many of those operations, which appear to be so plainly describ'd in books require something more, than a simple routine to execute.

How many varieties does the application of the trepan require? the accidents which render it necessary, the parts to which it is to be applied, & the number of applications, are so various, & different, that wee are frequently oblig'd to quit the plain beaten road, & boldly strike into a track entirely new, the propriety & necessity of which can only be discovered, by those Rules of Analogy, which are to be found in the structure of the parts, & the nature of diseases.

Is it not evident then that a clear, penetrating judgement, strengthened by

[7] Jones refers here apparently to Paré's reintroduction of the ligature in amputations, first described by him in his *Dix livres*, Paris, 1564.

[8] The surgeon was Félix de Tassy. For a detailed and rather amusing account of "La grande opération faite au Roi Louis XIV, en 1686" see the "Journal de la santé du roi Louis XIV de l'année 1647 à l'année 1711" by his chief physicians, Vallot, d'Aquin, and Fagon: Paris, 1862, pp. 166–175; 395–405.

a general sagacity, & extensive knowledge, more than a simply prescrib'd method, are necessary to conduct the hand of the operator? . . . There are also many cases, arising from the nature of wounds, & variety of diseases, which admit of no determinate mode from precepts; & where the assistance of the hand, can only be regulated, from the various attendant circumstances. . . . it is in these vari'd cases, that the utmost depth of the art of operating, consists.

An operation alone, is but a single point, in the cure of diseases; a just knowledge of the causes which require it, the accidents which attend it, & the treatment which must vary, according to the variety of these accidents, are the most essential objects in the art of surgery. And hence it will evidently appear, how necessary a deep knowledge of anatomy, & the animal oeconomy, is to the just exercise of this science. 'Tis this knowledge which lays the foundation, & constitutes a considerable part of the merit & difficulty of the art; & shews us from what hands, wee are principally to expect its progress.

The mind therefore must be prepar'd, before its entrance into the study of surgery, by a previous acquisition of those branches of knowledge, which teach us to unravel the operations of nature . . . without this preparation, wee can never arrive at a knowledge of those truths, which form the rules, by which wee ought to conduct ourselves, in the cure of diseases.

(1) 'Tis to such cultivated geniusses, that surgery owes its greatest progress—such were a Severinus, a Fallopius, a Hildanus, a Vesalius, a Scultetus, a Heister, a Le dran, a Wiseman, a Cheseldon, a Monro, a Sharp . . . these illustrious surgeons, whose minds were prepar'd by the study of the learn'd languages, cultivated by the belles lettres, & enrich'd with the knowledge of Philosophy, have hung up the best lights, to conduct us through the dark, & intricate windings of our art.

From this view of the Science the necessity & utility of a particular professor for Surgery will indisputably appear, & wee have already some reason to flatter ourselves that under the protection of the liberal patrons of the present medical institution, ignorance & imposture will be no longer able to combat truth & Error, & that the latest posterity may look back with gratitude on the benificent founders of an institution calculated to promote the health & happiness of mankind.

(2) To conclude Gentlemen . . . if the science of surgery, then, requires genius, knowledge, & indefatigable application, to render its Professors truly respectable! what must wee think of the insolence, & malevolence of those who represent it as a low mechanic art, which may be taught a butchers boy in a fortnight . . . yet such false & absurd representations, have been made of it, by some who have enjoy'd no small share of medical reputation in this country . . . & what is equally reproachful, there have been men who stil'd themselves gentlemen, ignorant & weak enough to credit such absurdities.

But we have some reason already to flatter ourselves that under the protection of the liberal patrons of this medical institution, Ignorance, & imposture will no longer be able, to combat truth & error, and that the latest posterity, may veiw with gratitude the benificent founders of an institution, calculated to promote the health, & happiness of Mankind.

Finis

Brief Outline of the Succeeding Lectures

The Introductory Lecture is to be regarded as Lecture 1, as the succeeding eight lectures are numbered 2 to 9. Their subjects are as follows:

Lecture 2 (20 pp.): the doctrine of inflammation in general. No authorities are cited.

Lecture 3 (24 pp.): the "inflammatory" tumors: phlegmon, abscess, anthrax, furuncle, erysipelas, shingles, glandular (breast, parotid or salivary, buboes, tonsils), paronychia or whitlow. Authority cited: Garengeot on Arnaut.

Lecture 4 (23 pp.): scirrhus, cancer, and struma. Authorities cited: Hildanus; Stoerck; Guy; Celsus; Tulp; Turner; Russell; Fothergill.

Lecture 5 (16 pp.): encysted and sarcomatous tumors: sarcoma, ganglion, bronchocele, hernias (bubonocele, etc.). Authority cited: Turner.

Lecture 6 (20 pp.): treatment of the various kinds of hernia; "spurious" hernias: sarcocele, hydrocele, emphysema; aneurysm. Authorities cited: Pott; Heister; Méry; Hunter (William); Le Dran. (This lecture contains the "case of hydrocele" printed by Mease in his edition of Jones' works.)

Lecture 7 (20 pp.): wounds in general; ulcers and their treatment. Authorities cited: Hippocrates; Sharp. (Jones later used the part on wounds in general as chapter 1 of his manual.)

Lecture 8 (18 pp.): ulcers with caries; burns; gun-shot wounds. Authorities cited: Ranby; Le Dran. (The section on gun-shot wounds appears as the first half of the 11th chapter of the manual. This lecture was evidently regarded as incomplete: a blank leaf separates it from the beginning of the next lecture; and three lines, ending abruptly, suggest the text as it is continued in the manual.)

Lecture 9 (24 pp.): fistula lachrymalis. Authority cited: Anel.

A Section Headed 'Operations'

There are several indications in the lectures that the didactic lectures were followed by practical demonstrations on the "dead subject". This section (12 pp.) headed *Operations* evidently comprises brief and inconclusive notes on points which the professor of surgery wished to bring out during the demonstrations. The notes refer to the following subjects: sutures; scirrhous and encysted tumors; amputations (leg, thigh, arm, fingers and toes, metatarsal bones); bubonocele, hydrocele; castration; trephining.

Comment

It has often been said that Jones' manual is merely a compilation from Ranby, Pott, and others, with but a single original observation. If that be so, these manuscript lectures, the "Introductory" excepted, have the great merit of presenting Jones in a far more effective light. Two impressions may be gained from even a casual reading of the lectures: one is of Jones as a surgeon well-versed in the literature of his subject; the other is of him as a keen critic and commentator, invariably weighing the dicta of others against his own experience. Nothing could be clearer than that he himself exemplified the qualities of the surgeon which he exalts in his Introductory Lecture. The lectures are replete with personal observation, no less than with learning and a high concept of the surgeon's task, and indicate that King's College was fortunate indeed in its selection of John Jones as its first

professor of surgery. This volume is without much question the sole surviving first-hand record of the earliest formal surgical teaching in New York.

Brief Outline of the Notes on the Lectures of William Hewson

The section headed *Operations* is unpaginated. Separated from it by a blank leaf, is a section, without heading, of 61 pp., the first 40 of which are numbered. The contents appear to be notes, partly worked-up into lecture form, on the lectures of William Hewson (1739–1774), the London anatomist and surgeon, interspersed with a few observations on the practice of other London surgeons.

Jones' biographers, dependent almost entirely upon their progenitor, Mease, are so reticent regarding the date of his second sojourn in England that it is difficult to assign these notes to a precise year. From Mease, one deduces that Jones returned to this country in 1774, after "a short stay", that seems, however, to have bridged two calendar years. Mease states that Jones "again attended the lectures of his old master Dr. Hunter, and those of his friend, Mr. Pott", but does not mention his attendance upon the lectures of William Hewson. Now, Hewson and William Hunter severed their partnership in the summer of 1772[9]. Hunter is not mentioned in these notes, as he almost certainly would have been, had Jones been attending their partnership lectures. It seems reasonable, therefore, to assign these notes to the winter 1772–3 or the winter 1773–4, with Mease's evidence lending greater probability to the latter. In that case, the notes would represent Hewson's last course of lectures.

The notes are on the following subjects:

1. Ruptures (5 pp.[10]). Lecturer indicated: Hewson.
2. Hydrocele and scirrhous testicle (4 pp.). Lecturers indicated: Else[11]; Warner[11]; Pott; Hewson.
3. Extirpation of the penis and phimosis, etc. (1 p.). Lecturer indicated: Hewson.
4. Lithotomy (7 pp.)[12]. Lecturer indicated: Hewson.
5. Suppression of urine (3 pp.). Lecturer indicated: none, specifically.
6. Fistula in ano (1 p.). Lecturers indicated: Hewson; Pott.
7. Paracentesis thoracis and bronchotomy (1 p.). Lecturer indicated: Hewson.
8. Wry-neck, hare-lip, and nasal polypus (2 pp.). Lecturer indicated: Hewson.
9. Cataract and fistula lachrymalis (3 pp.). Lecturers indicated: Pott; Warner; Hewson.
10. Trephining and aneurysms (3 pp.). Lecturer indicated: Hewson.
11. Amputation at the shoulder (2 pp.). Lecturer indicated: Hewson.

[9] George C. Peachey, "A memoir of William & John Hunter," Plymouth, W. Brendon & Son, 1924, p. 122.

[10] The number of pages given here, and below, does not include blank pages, or pages with headings, but containing no notes.

[11] Both Else and Warner had recently published on one or other of these subjects, and their opinions may have been taken from their publications; but the text seems to indicate that Jones had been in personal contact with them.

[12] Having in mind Jones' fame as a lithotomist himself, one is disappointed to find but one personal comment. In a footnote referring to Hewson's commendation of the "cutting gorget," Jones queries, "Might not a double cuting Gorget be preferable to a single one." Whether he knew of such an instrument invented and promulgated by the redoubtable William Bromfield is not clear.

12. Dissection and embalming (2 pp.). Lecturer indicated: none.

13. Gravid uterus (7 pp.). Lecturer indicated: Hewson.

14. Generation (4 pp.). Lecturer indicated: Hewson.

15. "Lecture 2d". Causes and cure of dropsies & particularly by the paracentesis (5 pp.). Lecturer indicated: Hewson.

16. Comparative anatomy (11 pp.). Lecturer indicated: Hewson.

Concluding Comment

It should be observed that the notes on Hewson, fragmentary as they often are, are not those of a callow student, or of a "servile imitator", either. Jones brought to his second course of study under the English masters an independent, inquiring spirit, governed by consciousness of his own not inconsiderable surgical experience; the notes so reveal it.

It is profoundly hoped that this introduction to an original manuscript of Jones' lectures will lead others to make better known the state of surgical teaching and practice in New York in a day which has left us few comparable records.

Memoir of William G. Spiller, M.D.*

By J. W. McConnell, M.D.

About one-hundred years ago, a cloth merchant of Baltimore, Maryland, by name Robert Miles Spiller, native of King William County, Virginia, married Miss Anne Augusta Maltby. On September 13, 1863, in Baltimore, a son was born to this couple, to whom was given the name William Gibson. At seven years of age this child was semiorphaned by the death of his mother and became partially dependent on his older sister until his father remarried. William was a quiet, somewhat retiring youngster, and hoping these peculiarities would be eliminated and the young man broadened in his general behavior, the father placed him in the Cheltenham Military Academy, at Ogontz, Philadelphia, the head of which institution, a certain Dr. Clemens, was a personal friend of the parent. Young Spiller attended school and, because he was not happy at home, spent most of his summers in the school atmosphere, under the influence of Dr. Clemens.

Robert Miles Spiller died when the son was fourteen years of age and William's guardian kept him at the Academy until he had completed that part of his education. This accomplished, the question arose—"what to do"? His roommate at the Academy was a popular fellow, highly regarded by young Spiller. This young man was L. Bolton Newbold who, on finishing school, went to North Dakota. Spiller went with him, purchased a tract of land and lived there for six years, the products of his farm being wheat and good health. While in Dakota he married Helen C. Newbold, the sister of his former roommate, and they remained in the West for two years.

During these twenty-four months, Mrs. Spiller increasingly realized that farming was not William G. Spiller's vocation. She believed his unusual mental makeup was the result, in part at least, of hidden student ability, which farming would not erase nor would it advance him. She, therefore, advised him to take up the study of medicine, and he entered the Medical School of the University of Pennsylvania in 1889, and graduated in 1892.

At Cheltenham Academy, during his years on a North Dakota farm, previous to and following his marriage, the trend of Spiller's mind was along the lines of rhythm and beauty. He read and wrote poetry, enjoyed good literature. He did a little painting, giving great attention to coloring. He was unable to pitch a tune or to play a musical instrument, but he was fond of music and enjoyed listening to performances on various instruments. He was especially fond of Shakespeare's works, which he reread and from which he could quote passages. He developed curiosity as to the whys and wherefores of phenomena. He learned to concentrate intensely. He completed his course at the University with highest honors and won the gold medal. Spiller had married the right woman. She recognized his asocial characteristics, his fondness for inquiry, his ambition to

* Scheduled to be read at the meeting of the College, November 6, 1940, which was cancelled; read December 4, 1940.

delve more deeply into the mysteries of science, and she advised him against taking an internship, which had been offered, and to pursue a different course.

Financially, he was able to do this and he went abroad and studied for three-and-a-half years. His original idea was the field of internal medicine, so, to acquire greater perfection, he went to England and spent three months investigating the clinics of London, searching for what he wanted. In that time he and Mrs. Spiller had fully determined his life work was among the specialties of medicine. Which one was the question, and, not finding the answer in London, Spiller went to Berlin and spent the most part of one year in the clinics, learning the language, acquiring knowledge, but not finding the niche he and his thoughtful wife felt he could fill. To Vienna he went, there to fall under the influence of Dr. H. Obersteiner. He obtained the privilege of working in Obersteiner's laboratory, attending clinics and watching his handling of patients in the wards. In the research laboratory he found an assistant, who did much of the detail work of preparing specimens for Professor Obersteiner. This young man, Otto Marburg, introduced Spiller to many of the intricacies of neuropathology, and, in the months spent there, Spiller became more and more interested in the clinical features of diseases of the nervous system, and greatly intrigued in the histopathology of those diseases. Two great neurologic scientists were working in Paris, the doctors J. J. Déjerine and his wife. To them Spiller applied for greater knowledge of his now accepted specialty; and he worked in their laboratory for part of a year. His leaving was sudden and dramatic.

During his absence from America, the Pepper Clinical Laboratory had been founded by the Provost of the University of Pennsylvania, Dr. William Pepper. He desired the best talent obtainable to carry on neurologic research work in that institution and he consulted with the Dean of Medicine as to the man best qualified for this position. The name of William G. Spiller was recommended to him. To find Spiller was somewhat difficult, but a messenger, Dr. Henry W. Cattell, sent by Dr. Pepper, eventually located him in Déjerine's laboratory in Paris. He was offered and accepted this new work.

Spiller's return to America, in 1896, was unheralded. He assumed charge of the newly established Research Department of the Pepper Laboratory, but he was not generally known in the neurologic world and scarcely recognized in the sphere of medicine. Following his return, one of his earliest visits was to the office of Dr. Charles K. Mills, and I had the good fortune to be present when he called and was allowed to remain during the interview between him and Dr. Mills.

Chronologically I was much younger than Spiller and I felt quite a youth as I listened to his recital of experiences in a world which to me was only known through reading. I realized why one man becomes enthusiastic about another, for Dr. Mills saw in Spiller a new order of things, a different line of work, an approach to an understanding of nervous diseases novel to him, who was regarded as most complete in his knowledge.

Within a short time, Spiller and I and others were working together in the Clinic for Nervous Diseases at the old Philadelphia Polyclinic, then located at 18th and Lombard Streets. Spiller introduced us to minor details, with resulting improvement in powers of observation. With the passing years, our personnel changed materially because

of the attraction which the combination of Mills and Spiller had for the beginner in neuropsychiatry, and for those studying specialties that were related to this branch of medical science. In a few years, 1903, Spiller was made Professor of Neuropathology at the University of Pennsylvania.

To list Spiller's activities would mean simply to repeat names of the outstanding institutions which vied with each other to obtain part of the service time of this scientist. His hospital affiliations were the Philadelphia General Hospital and the Hospital of the University of Pennsylvania, but, as a consultant, his activities went to many others in and around the city of Philadelphia. His name in a catalogue meant honor to the institution. His laboratory at the University of Pennsylvania grew to large proportions and was a museum of the pathologic specimens of nervous disorders. Research men were interested in it as the equal, if not the superior, of similar repositories at much older places of learning.

According to those who knew Spiller, previous to his return to Philadelphia in 1896, once he determined to study medicine that science appropriated all his waking moments. He studied most conscientiously; with great avidity he read material collateral to his lectures. He was keenly interested in the ill-defined small points of many things, the fundamentals of which were scarcely touched by teachers and lecturers. He became more of a teacher, still more of a student, and he developed many of the peculiarities of the grave professor. Finding a place where he would not be disturbed, selecting a certain room in his own home away from the common distractions of housekeeping and the entertainment of friends, he could pursue a line of thinking that would eventuate in the solution of some major problem. These individualisms were apparent in his study of cases at the University Hospital or at the Philadelphia General Hospital, where he would locate himself, and his associates, at a bedside, screened from disturbing factors, and examine the patient with a thoroughness not employed by many men.

The state of mental abstraction possessed by Spiller was rarely not present. Sometimes it was a source of amusement. One first day of January, accompanied by his daughter, he called at the residence of Dr. Charles K. Mills. He was greeted with the usual holiday wish and Dr. Mills asked Miss Spiller, "Is your father taking you to see the mummers"? "Mummers", answered Spiller, "what do you mean, mummers"? "Oh, I mean the parade on Broad Street in celebration of New Year's Day", answered Dr. Mills. "Oh, no, no", said Spiller. "Well", said Dr. Mills, "I thought Helen might enjoy it". "Oh, no", responded Helen, "Father thinks I will enjoy, much more, seeing him change the fluid on his laboratory specimens".

On another occasion, Spiller was asked by one of the staff at the University Hospital—"What would you choose to do as a vacation"? "Well", said Spiller, "I would like to take a thousand or more of my slides and be undisturbed while I reexamined them".

For quite a while Spiller denied private patients access to his valuable knowledge of diseases of the central nervous system. This was due to his abhorrence of publicizing himself. Even consultations were accepted by him only under strong urging. Eventually, he relented; obtained office accommodations away from hospitals and began his career as a practitioner of neurology. His consult-

ing room was in modest quarters on Chestnut Street near Twentieth. In entire harmony with his personal characteristics, the furnishings were adequate, rather austere, nothing suggestive of great comfort or of permanency. A fellow occupant was a younger neurologist. This arrangement was mutually agreeable and as the men presented personalities diametrically opposite the association was well balanced and continued for several months.

To the casual observer, Spiller was a sympathetic, gentlemanly doctor. To those of us who were more imtimate with him, seeing him under the stress of a busy clinic and of large professional obligations, Spiller had most remarkable patience and control of temperament. He never used strong language nor did he elevate his voice. His habits were immaculate. He never used tobacco and rarely did he indulge in alcoholic liquors. Yet with all these moral qualities, Spiller was not lacking in the humanness one does not always find in the individual minus what is denominated the "physical contacts with other people". One day in his dispensary, Spiller overheard an assistant giving advice to a half-starved, weak-looking patient. "Now", said the assistant, "you get this medicine at the drug counter; go home, fix yourself a thick, juicy beefsteak, broil it and have potatoes, some vegetables, and good coffee, and when you put them under your belt you'll feel a great deal better". "Doctor", chimed in the unobserved Spiller, "don't forget to give the man the price of all that, he looks as though he might need it".

Spiller's contributions to scientific literature numbered in the hundreds. They were theoretic, practical, clinical, constructive. A few were revolutionary. He regarded as productive of his most important practical results, the personal and consulting work with Dr. Charles H. Frazier, in which painful and other diseases of the fifth nerve were considered. All clinical work was grist to the scientific mill. His presidential address before the American Neurological Association, in 1905, was upon "The Importance in Clinical Diagnosis of Paralysis of Associated Upward Movements of the Eyeballs, Especially the Upward and Downward Associated Movements".

The completeness of his knowledge of physiology and anatomy, and his ever present desire to relieve suffering, led Spiller to suggest to Dr. Edward Martin the operation of cordotomy as a theoretic and experimental procedure for the relief of pain and of spasticity of muscles. Later, with Dr. Frazier, he elaborated this method of treatment. He collaborated with Dr. William C. Posey in the preparation of "The Eye and the Nervous System". Always, his literary productions were well conceived, meticulously honest, loaded with facts.

Spiller's earliest attempts at teaching clinical neurology not infrequently resulted in a confused presentation, difficult for the average student to understand. With the passing of time and frequent personal contacts with the students, his demonstrations and lectures became more interesting. Questions from his students and by his associates helped to develop in him the systematic, analytic clinician who furnished those seeking information on neurologic subjects convincing proof of his keen knowledge of the subject and his ability to impart it to others, showing them how and why he arrived at conclusions.

He was most enthusiastic in clinical work, constantly on the hunt for new symptoms or clues. Occasionally this search led him into minor errors which,

on cooler thought, were corrected. As his chief of clinic for many years, one of my duties was to provide and prepare material from the outpatient department for his clinical lectures at the University of Pennsylvania. A particular example of the result of his overflow of interest and at the same time his ability to turn a mistake into something of teaching value is the following:

Dr. Williams B. Cadwalader and I had studied an instance of acute anterior poliomyelitis, which involved the left leg in a very selective manner. The diagnosis was not written upon the card, awaiting, as was the rule, Spiller's final decision. On this occasion, seeing the patient, he expressed his joy at observing for the first time in his life a pure motor sciatica, and he wished to exhibit it at his clinic. We examiners were chagrined that Spiller catalogued the patient under this unusual title, but so he signed it. When the clinic day arrived and Spiller saw the card with the diagnosis he said, "Why, whoever made this diagnosis"? Quietly I said to him, "Why, Dr. Spiller, that is your handwriting". "Oh", said he, "I don't think I could ever have been so foolish, this is nothing but a case of infantile paralysis, of spinal type". However, he used the case and presented it very elaborately as a text for possibility of errors in diagnosis.

With all his abstractiveness, not infrequently Spiller responded to an innate sense of humor which many people felt did not exist in him. An incident occurred at the office he shared with one of his confreres who was much given to the lighter things of life. I happened to be in the room and the telephone bell sounded. Spiller, sitting at the desk, responded. Just what the conversation was neither the associate nor I knew at the moment, but Spiller's flushed face showed his confusion. He asked the speaker to repeat what was said. This done, he excused himself and handed the telephone over to his officemate, saying, "I think this must be for you". When the officemate had the message repeated, he broke into hearty laughter. Further conversation was one-sided but appreciated by the listener, who eventually hung up the receiver. Spiller then apologized and said, "I don't know of anyone who would address me that way but when the young lady said, "You don't love me", I knew it could only be for you".

Religion as a formality did not appeal to Spiller. It was something belonging to him personally; it did not relate to sect; it had nothing to do with fundamentalism or modernism. He seemed always to exemplify the teaching probably given to him in his youth, of practicing obedience to the "ten commandments", following the "golden rule", and having ample charity in his makeup for all necessities.

His family consisted of four children and in his contacts with them there was an absence of the scientific man and the marked presence of fatherly interest. I recall, with distinctness, Spiller's anxiety when his daughter was ill with typhoid fever. It was so great that, with difficulty, we were able to get him to pay attention to the work of the neurologic department of the University of Pennsylvania. The education of his children was an important feature of his life and he lived to see all of them successfully graduated from their selected institutions of learning and on their respective ways to the consummation of their desires.

The purpose of a personal memoir is to summarize the noteworthy events in the individual's life. At times the memorialist attempts to calculate the influence

of the one memorialized upon the future. In an effort to do this, in respect to Spiller, the writer's close association, for thirty-nine years, does not make less difficult the task, properly, to evaluate him, during his lifetime, or, after his death, correctly to estimate the worth of Dr. William G. Spiller to his particular art or to his profession.

He lived and practiced neuropsychiatry in the chronology of the pioneers of that specialty and through the post-war era. His laboratory and clinical experiences proved and clarified the labors of Mitchell, Mills, Dana, Parker, and others, and linked their work with developments from research in the biology, the chemistry, the electrodynamics, the mechanics, and the synthetic therapeutics of the diseases of the nervous system, as exemplified by Kappers, Sherrington, Head, Adrian, Fulton and many more. We can appreciate his wisdom, his work, his methods, and his results. We regard the respect in which he was held by friends, by students, by brother practitioners, and by people generally. But adequately to review all of the salient features of his life and successfully to draw conclusions would require the possession of a memory free from vagueness, an emphasis on major and minor things that is perfectly placed, a well balanced personal equation, and then, the sum total of success would vary with different estimators.

Certain impressions made by Spiller on the writer stand out very prominently in his mind. From 1896 to 1935, Spiller developed steadily and smoothly from the retiring, contemplative student and the absorbed scientist, to the neuropsychiatrist who thoughtfully employed experimental and theoretic procedures, to relieve pain and restore function. At all times he believed the successful accomplishment of such procedures resulted only from persistently keeping in contact with the most recent developments and illuminating new thoughts, whether they came from those engaged in work similar to his or emanated from those who thought they were performing along the same lines. He accepted advice from lay experimenters, and suggestions based upon legend and old wives' tales. His memory was astonishing, his ability to grasp facts was marvelous. Some of the results of these faculties we have tried to relate in the foregoing text.

After his retirement from active service, he enjoyed maintaining touch with advances in neurology and psychiatry and particularly he appreciated the visits of his coworkers and friends, who would discuss with him matters relating to his heart interest. Gradually the physical man disintegrated, the mental ceased to respond. His death occurred on March 18, 1940, in the Hospital of the University of Pennsylvania, the one place of which he was most fond, a perfect setting for the departure of the man whose greatest work was done within the shadows of its walls.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

Regular Meeting, October 28, 1940

The Dosage of Thiamin Chloride (Vitamin B_1) As Determined by OBT Titration of the Patient's Blood Serum. David L. Farley, M.D. (*Abstract 1, below.*)

The Importance of Gastroscopy in Differentiating Gastric Lesions. C. Wilmer Wirts, Jr.*, M.D. (*Abstract 2, below.*)

The Diagnosis of Carcinoma of the Pancreas. J. Edward Berk*, M.D. (*Abstract 3, below.*)

Testosterone Therapy in a Case of Metastatic Adenocarcinoma of the Ovary. Anna P. Klemmer*, M.D., and Roland N. Klemmer, M.D. (*Abstract 4, below.*)

Regular Meeting, November 25, 1940

The Behavior of the Blood Sedimentation Rate during and after Fever Therapy. Ferdinand Fetter, M.D., and Truman G. Schnabel, M.D. (*Abstract 5, below.*)

A Clinical and Pathological Report of an Unusual Case of Chronic Pneumonitis. Simon S. Leopold, M.D., and Warren F. Sheldon*, M.D.

Epidemic Influenzal Pneumonias: Their Characteristics as Altered by Various Complicating Infections. Robert G. Torrey, M.D. (*Abstract 6, below.*)

Body Temperature and Its Relation to Neurocirculatory Asthenia (Soldier's Heart; Effort Syndrome). Hobart A. Reimann, M.D. (*Abstract 7, below.*)

* *By invitation.*

Abstracts

1. The Dosage of Thiamin Chloride (Vitamin B_1) as Determined by OBT Titration of the Patient's Blood Serum. David L. Farley, M.D.

I have found a biological method which estimates the quantitative effect produced in the blood by the administration of thiamin chloride. (Bull. Ayer Clin. Lab. Nov. 1939, p. 331.) The principle of this method is the determination of the power of the serum to stop hemolysis of sheep cells by digitonin. The term OBT was coined by me as an equivocal name of the substance in the blood serum which inhibits hemolysis. The results of the test are given in terms of dilution. The power of the serum of 100 normal persons was determined, likewise that of 40 rabbits.

Suggestion of Dosage: Despite experience in the administration of thiamin chloride, I am still uncertain as to the best dosage. It has seemed to me that the effect varies so much in a sick individual that reliance for the proper dosage must be gauged by the effect produced in the serum. It has seemed that a titration of at least 5000 by our method must be reached before any striking improvement occurs. The titration of 2000 may be sufficient for the needs of a normal person but in one not in good health the higher figure of 5000 seems more preferable. I have based my conclusions on dosage by milligrams rather than by units. Ten milligrams daily in most sick

individuals seems to be enough to produce results. In some cases 50 milligrams daily seems to be necessary to raise the titer of the serum to 5,000. A striking phenomenon has been that three days must elapse when the drug is given by mouth before any effect can be observed in the serum.

Conclusion: The administration of thiamin chloride (Vitamin B_1) causes a quantitative increase in a substance in the serum which inhibits hemolysis of sheep cells by digitonin. It is suggested that estimation of the level of this inhibitory power may be useful as a measure of the dosage of thiamin chloride.

2. The Importance of Gastroscopy in Differentiating Gastric Lesions. C. Wilmer Wirts Jr*, M.D.

The presentation is based upon a group of patients having either gastric cancer or gastric ulcer, in which gastroscopic examination was the chief means of making a definite diagnosis. The patients were not seen consecutively but were selected to emphasize the role played by gastroscopy and in each case roentgenological and gastroscopic studies had been made during routine ward or clinic observation.

Fourteen patients with gastric ulcer are discussed. In nine of these patients roentgen-ray examination suggested that the lesion was "probably malignant", in two cases that it was "probably benign" and in three patients no gastric lesion was seen. In each of these fourteen patients a benign ulcer was diagnosed gastroscopically, the diagnosis being confirmed at operation in three instances, and by improvement on medical management and disappearance of the lesion gastroscopically, in the remaining eleven patients. The histories of two cases of gastric ulcer are given in detail.

In the group of cancer patients twenty patients are discussed and the detailed histories of three patients given. Of these twenty patients eleven were diagnosed as "probably", or "possibly", malignant, roentgenologically, and nine were reported as having no gastric lesion. In each of these twenty patients gastroscopic examination revealed a malignant lesion of the stomach. Sixteen of these patients came to operation and malignancy was found on histological examination, two were diagnosed as carcinoma on peritoneoscopy, one refused operation and one was considered a poor surgical risk because of advanced diabetes mellitus. Two of the case histories in this group demonstrate that the malignant character of a lesion is sometimes more apparent gastroscopically than grossly. Ten colored slides were shown, demonstrating the gastroscopic appearance of the lesions discussed, together with a picture of the roentgen-ray films in each case.

3. The Diagnosis of Carcinoma of the Pancreas. J. Edward Berk, M.D.

A poll was taken among 120 recent medical graduates representing 34 different medical schools on the question of their outstanding diagnostic impressions of carcinoma of the pancreas. Jaundice was selected by 92½ per cent as the outstanding and commonest feature of the disease, and approximately half of this group specified further that the jaundice was painless in type. Only 2½ per cent felt that pain ranked as the predominating characteristic.

An analysis was made of 34 cases of primary carcinoma of the pancreas

* From the Bronchoscopic and Gastrointestinal Clinics of Jefferson Hospital, Philadelphia, Penna.

proven by laparotomy or necropsy, and the results were combined with similar reviews previously reported in the literature.

Pain was shown to occur earlier and more frequently than jaundice and was the outstanding symptom. Painless jaundice proved to be relatively infrequent. Some derangement in carbohydrate metabolism, x-ray abnormalities and elevated concentrations of the pancreatic enzymes in the blood were findings of invaluable aid in the diagnosis of carcinoma of the pancreas.

It is necessary to revise our present conception of carcinoma of the pancreas. The traditional picture of painless jaundice and palpable distended gall-bladder is seen in somewhere between 25 and 40 per cent of cases and when present is, of course, significant; but, unfortunately, the majority of cases do not present this syndrome. Fatty stools are rare.

4. Testosterone* Therapy in a Case of Metastatic Adenocarcinoma of the Ovary. Anna P. Klemmer, M.D., and Roland N. Klemmer, M.D.

A female, aged 64, at operation 9–21–30 showed ascites with generalized abdominal metastases of an ovarian adenocarcinoma, confirmed by omental biopsy. She received 3200 r of abdominal irradiation, before hospital discharge. Beginning 11–6–39 her treatment was testosterone propionate only, by subcutaneous injections, a total of 12,220 mg. in 12 months. Her health improved for one year and although the abdominal tumors probably increased in size, the ascites disappeared.

Three months after testosterone was begun she was nearly bald. By another month new hair began to grow and soon she was so delighted with the new brown hair that she was willing to endure her deep hoarse voice. The clitoris is definitely enlarged and there was finally a definite hairy growth on the face but no masculine distribution on the trunk.

Intestinal obstruction began 9–12–40. Beginning 10–1–40 she received 300 mg. of testosterone daily for 18 days. Repeated blood calcium and blood counts were normal.

Dr. Olive Hoffman conducted hormone assays on urine collected 10–12–40 and 10–13–40, which was during the intensive testosterone treatment. Estrogens totalled at least 150 mouse units daily; androgens 62.9 mg. and 78.1 mg. (consecutive days); and follicle stimulating hormone 250 Levin and Tyndale units daily.

Animal and human experimental work suggesting a possible therapeutic value for testosterone in carcinoma was considered.

Our patient was apparently not harmed by the large doses of testosterone. On the contrary, it seemed to contribute temporarily to her comfort and we believe that further similar experimental trial is not contraindicated.

5. The Behavior of the Blood Sedimentation Rate during and after Fever Therapy. Ferdinand Fetter, M.D., and Truman G. Schnabel, M.D.

In order to find out if physically induced fever alters the blood sedimentation rate, a study was made of the behavior of this test during and after fever therapy. Forty-one patients suffering from general paresis, rheumatoid arthritis, gonococcal arthritis, Syndenham's chorea, ulcerative colitis, rheumatic fever, or multiple sclerosis, and who were being

* Testosterone Propionate (Oreton) supplied through the kindness of Dr. W. H. Stoner, of the Schering Corporation.

given physically induced fever in the hypertherm, were used in the study. Erythrocyte sedimentation rates (using the small Cutler tube) were determined on each patient 4 times; before fever therapy, during the height of the fever, as soon as the temperature had returned to normal, and the day after fever therapy. The sedimentation rates in these patients varied from 3 mm. in 1 hour to 31 mm. in 1 hour. However, there was very little variation in the sedimentation rates of any 1 patient's blood in the 4 determinations made. The usual variation was 2 to 3 mm., and the maximum variation was 6 mm. The averages of the sedimentation rates in the 4 determinations on the 41 patients were: before fever therapy, 17.8 mm.; during fever therapy, 18.9 mm.; immediately after fever therapy, 17.4 mm.; and the day after fever therapy, 19 mm. Since physically induced fever used therapeutically does not affect the blood sedimentation rate, an accurate determination of this can be done at any time during or after a fever session.

6. Epidemic Influenzal Pneumonias: Their Characteristics as Altered by Various Complicating Infections. Robert G. Torrey, M.D.

The probability of a pandemic in the near future makes a review of the observations made during the 1918 epidemic and of recent research on influenza virus important at this time.

Uncomplicated influenza is a relatively mild disease, the virus of which rapidly invades the entire respiratory tract, attacking the epithelial lining of the nose, sinuses, bronchial tract and air sacs. During a few days before epithelial repair is established this provides a perfect culture medium for rapid bacterial spread. In this stage any of a number of organisms will cause a diffuse bronchopneumonia. The pneumococcal strains, streptococcus hemolyticus and Pfeiffer organism spread rapidly throughout the entire respiratory tract. Hard coughing strains the weakened lung structures and causes acute emphysema which is a characteristic feature of these pneumonias. (The pathological features of the pneumonias produced by these various organisms in the presence of virus infection is illustrated by slides.)

The virus infection is transitory and epithelial repair very rapid. There is hyperplasia of the bronchial epithelium and the new cells are resistant to invasion. Pneumococcic pneumonia in this stage assumes a lobar form and streptococcic bronchopneumonia is not apt to appear.

A feature of flu pneumonia is a moist film in the alveolus which allows the blowing off water soluble CO_2 but prevents the entrance of oxygen, thus giving the characteristic picture of intense anoxemia without a corresponding degree of subjective dyspnoea.

Aside from empyema and abscess, the important sequelae of influenzal pneumonias are alveolar emphysema and fibrosis. Prolonged anoxemia causes neuro-circulatory asthenia. Chronic sinus infection, particularly of the ethmoid and sphenoid cells, is usual.

While treatment in the last epidemic was unsatisfactory, the recent success with sulfonamide drugs in the handling of pneumococcic and hemolytic staphylococcic infections, which were in the past the most serious and prevalent secondary invaders, makes it seem probable that these complicating infections may be materially checked. Unlike anti-sera, synthetic chemicals can be produced in

quantity and thus be available for use in a pandemic.

It is important to limit the severity of the cough by sedatives, as hard coughing causes serious damage of the lung structure weakened by virus infection.

7. Body Temperature and Its Relation to Neurocirculatory Asthenia (Soldier's Heart: Effort Syndrome). Hobart A. Reimann, M.D.

Although the average oral temperature of most normal persons is 37 C. (98.6 F.) there exist many apparently well persons whose average temperature is considerably lower or higher. Not all of these persons, however, are actually "normal", for many of them have evidence of slight imbalance of the pulse rate, blood pressure, basal metabolic rate and often have the signs and symptoms of a neurosis. In general, most of the persons studied whose temperature was continuously higher than 37 C. (98.6 F.) were women in whom the height of the temperature elevation was related to the menstrual period. Their whole symptom-sign complex generally fitted into the condition called sympathicotonia. On the other hand, all persons thus far studied whose temperature was consistently subnormal were men who could be classed as vagotonic. In both cases the evidence of either sympathicotonia or vagotonia was incomplete and usually there was a mixture of signs of both conditions in the same person with a predominance of one over the other. (J. A. M. A. 115:1606–1609 (Nov. 9) 1940.)

The vagotonic men studied seemed to fit perfectly in the class of patients said to have neurocirculatory asthenia or soldier's heart. These terms, then, if actually a part of general condition should not be applied to indicate a disturbance of one organ or system alone. The signs and symptoms in all patients should be integrated and correlated into one syndrome, thus avoiding much needless investigation and unnecessary treatment. It must also be borne in mind that vagotonic or sympathicotonic patients may actually have other disease as well, but in any case the underlying constitutional makeup of the person has a strong influence on the patient's reaction to any stimuli or abnormal circumstances.

SECTION ON MEDICAL HISTORY

Regular Meeting, November 11, 1940

Erasmus Darwin: A Character Study. Robert L. Pitfield, M.D.

The Rôle of the Spanish Mission of California in Early American Medicine. (Illustrated by motion picture in color.) William G. Leaman, Jr., M.D.

Regular Meeting, December 9, 1940

(Annual Students' Night)

Philadelphia Hospital Units with the A. E. F.: Their History, Organization, and Activities. *Pennsylvania Hospital, Base Hospital No. 10.* Charles F. Mitchell, M.D.; *University Hospital, Base Hospital No. 20.* Alexander Randall, M.D.; *Jefferson Hospital, Base Hospital No. 38.* Clifford B. Lull, M.D.

SECTION ON OPHTHALMOLOGY[1]

Regular Meeting, October 17, 1940

Pneumococcus Infection of the Conjunctiva Followed by Pneumococcus Meningitis: A Case Report.

[1] The transactions of this section are abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology*.

Carroll R. Mullen, M.D., and Joseph R. Weintraub*, M.D.

Microphthalmus with Tumor-like Glial Proliferation. Wilfred E. Fry, M.D.

Orthoptic Training as an Adjunct in the Treatment of Squint. George E. Berner*, M.D.

The Surgical Treatment of Neurofibromatosis (Plexiform Neurofibromata). Edmund B. Spaeth, M.D.

Regular Meeting, November 20, 1940

(The Third Annual de Schweinitz Lecture)

Occlusion Hypertropia. Frederick H. Verhoeff*, M.D.

SECTION ON OTOLARYNGOLOGY[2]

Regular Meeting, October 16, 1940

Vincent's Ulceration of the Soft Palate: A Case Report. Karl M. Houser, M.D.

Refractive Multiple Sinusitis: A Case Report, with Observations on Sulfanilamide Treatment. Kelvin A. Kasper, M.D.

An Unusual Foreign Body in the Nose Identifiable Only by X-Ray: A Case Report. Joseph C. Donnelly, M.D.

Extensive Mastoid Infection without Symptoms or Local Signs: A Case Report. Edward H. Campbell, M.D.

Aberrant Salivary Gland in a Faucial Fossa: A Case Report. William J. Hitschler*, M.D., and Thomas A. Cope, Jr.*, M.D.

Regular Meeting, November 20, 1940

Non-Surgical Treatment of Sinusitis

Anti-Allergic Therapy. Richard A. Kern, M.D.

X-Ray Therapy. B. P. Widmann, M.D.

Vaccine Therapy. Myer Solis-Cohen, M.D.

Local Therapy. H. P. Schenck, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

Regular Meeting, October 7, 1940

(Chairman's Address)

The Tuberculosis Problem in Philadelphia. Maurice S. Jacobs, M.D.

Meeting, November 8, 1940[3]

Medical Preparedness

Blood Storage and Shock. (Mary Scott Newbold Lecture XLVIII.) Francis John W. Roughton*.

A Health Program for the Homeside in Wartime[4]. Arthur Parker Hitchens, M.D.

* *By invitation.*

[2] The transactions of this section are abstracted in the *Archives of Otolaryngology*.

* *By invitation.*

[3] Joint meeting with the College.

[4] Printed in this (December, 1940) number of the *Transactions & Studies*.

TRANSACTIONS & STUDIES

of the

College of Physicians of Philadelphia

Volume 8 (Fourth Series)

Number 4 (February 1941)

Recent Studies in the Circulation of the Portal Bed and of the Spleen in Relation to Splenomegaly*†

By Allen O. Whipple, M.D.

FOLLOWING Malpighi's (1) classic description of the anatomy of the mammalian spleen, there has been a recurrent controversy among anatomists regarding the histology of the vascular bed of that organ. Proponents of an open circulation claimed that there was no continuity between the terminal arterioles and the venous sinuses, but that the splenic pulp spaces provide the only link between the arterial and venous radicals. Equally emphatic in their opposing claims have been those who maintained that the arterioles emptied directly into the venous sinuses and that the vascular bed was a closed system. Modern opinion rather favors a combined type of circulation in the mammalian spleen, that is, an open component in the vascular bed which permits the flooding of the splenic pulp spaces with whole blood but with additional pathways available, by means of which the extravascular detour of the pulp spaces may be short-circuited by direct communications between the arterioles and the venous sinuses. Whether these arteriovenous connections of which it is composed are structurally intact vascular tubes or whether their appearance may be accounted for on a purely functional basis, such as an alteration in the porosity of the pulp caused by contraction of the splenic musculature, is considered to be an open question.

The reasons for this three-sided debate have been the difficulty of interpreting the intricate patterns of the spleen as seen in microscopic sections stained by different methods and the varying results obtained by the several techniques of injecting the vascular bed of the spleen both by artery and by vein.

In 1931 McNee (2) reported that "in the direct observations of the thin edge of a mouse's spleen, examined with a dis-

* Thomas Dent Mütter Lecture LIII, The College of Physicians of Philadelphia, December 4, 1940.

† From the Department of Surgery, Columbia University, and the Spleen Clinic, Presbyterian Hospital, New York, New York.

secting microscope and very powerful light, erythrocytes could be seen lying stationary in the pulp while blood was pumping freely through the adjacent arterioles into sinuses and then emerging by the veins." No one made use of this valuable suggestion in method until Knisely (3), working in the Hull Laboratory in the University of Chicago, published his studies on transilluminated living spleens. He described the finest structural and functional details of the vascular bed and his account of them was expressed in no uncertain terms. His conclusion that the "unstimulated splenic vascular system of mice, rats and cats consists of a system of preformed, interconnected lined channels," normally intact and permitting the egress of only the fluid content of the blood, presented the most convincing argument in favor of the hypothesis of the closed circulatory mechanism in the spleen. He maintained that trauma incidental to manipulation, injection and fixation of the spleen had been responsible for the antagonistic studies of histologists in this field.

Knisely's positive description of the visualized functioning circulation in the spleen and his graphic drawings of the venous sinuses in what he termed the three phases of filling, concentrating and emptying of red blood cells, with sphincters at the entrance and exit of the sinuses were so convincing that several writers on the subject of splenic circulation have recently accepted his claims without question. Von Herrath (4), in his paper published in 1938, speaks of the "hematocrit function" of the venous sinuses as demonstrated by Knisely. But no one, until we began this study, had repeated Knisely's observations or corroborated or questioned his conclusions.

Because many of the problems in the pathology and clinical manifestations of the splenopathies depend upon a knowledge of the exact mechanism of the circulation in the spleen, the members of the Spleen Clinic at the Columbia-Presbyterian Medical Center were especially interested in Knisely's papers (3). We visited the Hull Laboratory on two occasions and later sent one of our Surgical Residents, Dr. David W. MacKenzie, Jr., for a period of four months to study with Dr. Knisely. He most kindly gave Dr. MacKenzie every opportunity and on his return to our laboratory the apparatus and method were set up for studying the transilluminated spleen.

Before studying abnormal spleens it was essential for us to become thoroughly familiar with the circulation in the normal spleen. It had become apparent to Dr. MacKenzie that two fundamental faults in Knisely's technique made a continuous uninterrupted study of vascular fields impossible: the first and most misleading was the constantly moving visual field caused by the respiratory movements transmitted to the spleen under the microscope; the second was the frequent displacement of the spleen with the movements of the animal when the sodium amytal anesthesia was repeated by hypodermic injection. By devising a celluloid supporting table for the spleen and by using a continuous clysis of sodium amytal solution these two causes of a shifting microscopic field were eliminated and it became possible for the first time to observe areas of the vascular bed in the immobilized organ without any shift in the visual field over uninterrupted periods of several hours. Before this was done, the necessity of filling in gaps between the views of the vascular bed we feel was the cause of fundamentally wrong observations and conclusions.

We regret, therefore, that we are unable to corroborate many of Knisely's findings

and are compelled, as a result of a year of study, to differ positively from him in his conclusions that the circulation is a closed circulation and in the three phasic functions he attributes to the venous sinuses. Our observations were made by at least three, and sometimes more, members of the Spleen Clinic and the investigation. While we are impressed by the importance and the value of transillumination in the field of histo-physiology and histo-pathology, we wish to curb the enthusiasm of those who would undertake this technique in the study of living tissues. Transillumination carries with it definite limitations.

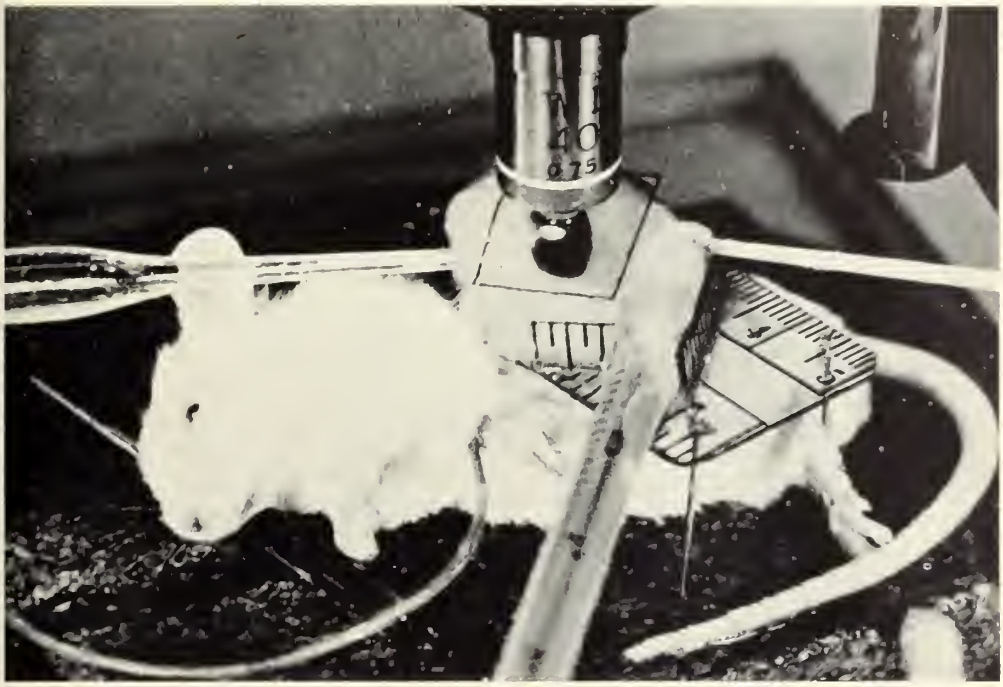

Fig. 1. Transillumination Apparatus Arranged for Observation of an Exteriorized Mouse Spleen

Hollow-tipped, fused quartz, illuminating rod enters spleen chamber from left; immersion fluid delivery tube from right; and thermometer from foreground. Anesthesia fluid is being conveyed to this animal's left pectoral region. Light from illuminator tip is directed upward, through spleen substance, into water-immersion objective.

anatomical components or structures of the vascular bed have been recorded by camera lucida drawings of the functioning fields studied by us over periods of one or more hours in the living transilluminated spleen of mice, rats, kittens and guinea pigs.

We wish, as a preface, to record our qualification of the method used in this Refraction difficulties inherent in the observation of untreated living tissues are great and in some respects as yet insurmountable. The relatively fluid state of the parenchymatous organs and consequently minimal differences in refractility among the component tissues make the differentiation of anatomical and functional zones a matter of con-

siderable difficulty, in which the subjective factor can alter the objective in even the most conscientious individual observer. We have made standard histological sections of the spleens studied

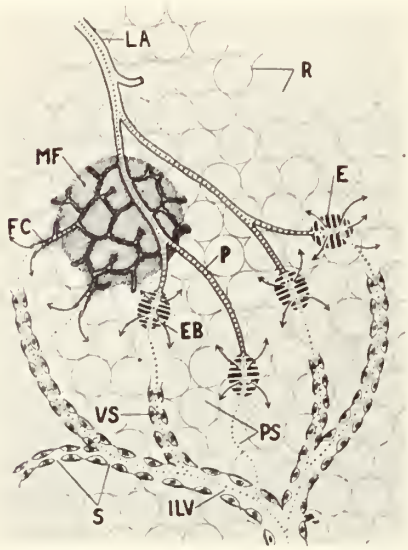

Fig. 2. Diagram of the Intralobular Circulation in Certain Mammalian Spleens (e.g., that of the Cat), as Suggested, in Part, by McNee's (1931, Fig. 6) Representation of a Splenic Lobule.

Arrows radiating from ellipsoids and follicle capillaries suggest a few of the innumerable pathways by which blood may traverse the pulp interstices in relaxed or distended spleens, and emphasize the morphologically 'open' character of the circulation. Dotted lines indicate the short-cuts taken by most of the blood when the circulation is functionally 'closed' by splenic contraction.

LA, lobular artery; *MF*, Malpighian follicle; *P*, penicillus; *FC*, follicle capillary; *E*, ellipsoid; *EB*, lateral channel in wall of ellipsoid; *R*, red pulp reticulum; *PS*, pulp spaces; *VS*, venous sinus; *ILV*, intralobular vein; *S*, stigmata in walls of venous sinus and intralobular vein.

and compared these with those of recognized authorities in our interpretation of the transilluminated fields. Nevertheless, when one becomes accustomed to the refraction patterns, transillumination of living functioning structure provides a unique and fascinating method for histological study.

At this point I wish to say that by far the major part of this study of the vascular bed of the spleen, the improved method and techniques, the continuous observations and the drawings, both free hand and camera lucida, were made by Dr. MacKenzie and by his able assistant, Mrs. Wintersteiner. The detailed report of this study by MacKenzie, Whipple and Wintersteiner (5) is in press and will appear shortly in the *American Journal of Anatomy*. I have used some of this material as a basis for a possible explanation of some of the splenopathies by correlating the pathological with the clinical picture of these splenopathies.

The storm center in the controversy over open or closed circulation in the spleen has had to do with the question as to whether the arterial capillary terminates freely in the reticular meshes of the pulp spaces or directly into the venous sinuses. This question must be answered positively if certain essential points regarding the pathogenesis of many of the splenopathies are to be settled.

It is our definite conviction from our studies in the living spleen, which are in agreement with the conclusions of Mall (6), Robinson (7), Foot (8), and Klemperer (9), among others, from injected spleens and from microscopic sections, that the splenic pulp spaces provide the one and only link between the arterial and venous systems in the mammalian spleen. Individual pulp spaces are the most variable structures that we have observed in the spleen. For the most part they are tortuous, utterly irregular and inconstant channels, lined by fixed and wandering cells and by reticulum. They constitute a plexiform, three dimensional system of channels intimately

connected with one another by actual or potential passages, fully adequate to transmit the cells as well as the fluid of the blood. The average width of the pulp spaces in the normal relaxed spleen of the mouse is 6 microns, but the diameter of a dilated pulp space has been measured at 16 microns. A collapsed or compressed space may have no visible lumen. On the arterial side of this fibrocellular sponge the pulp spaces communicate with the arterial capillary ampullae, or ampullae of Thoma. On the venous side, the spaces converge upon the stigmata or free openings of the venous sinuses and intralobular veins. Camera lucida drawings of this intermediary zone and of the pulp connections with arterial and venous systems are shown in Figures 3–6, and are in agreement with the semi-diagrammatic drawing of the intermediary circulation in the human spleen (Figs. 7–11) as represented by Klemperer (9).

Fig. 3

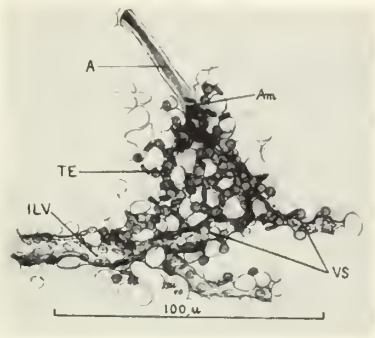

Fig. 5

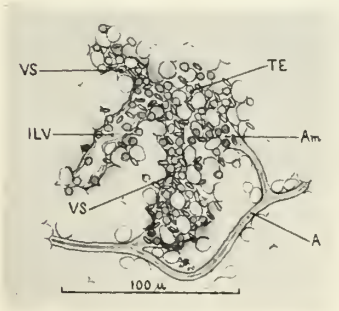

Fig. 4

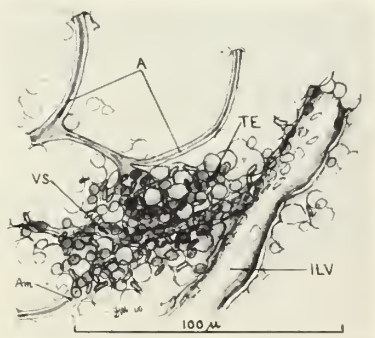

Fig. 6

Figs. 3–6. Intermediary Circulation in Transilluminated Mouse Spleens

Arterial capillaries, *A*, are shown to communicate via ampullary dilatations, *Am*, with swamp-like pulp zones, through which erythrocytes trickle onward, *TE*, into venous sinuses, *VS*, and intralobular veins, *ILV*.

Camera-lucida drawings. Lens magnification of figs. 3 and 4, 400; of figs. 5 and 6, 600.

It is in our visualization of this inter-

mediary circulation that we differ so definitely from Knisely's views of the venous sinuses, which he claims are closed connecting links between the arterial capillaries and the intralobular veins. For it is in the splenic pulp spaces that free blood circulates and the blood is stored or filtered for varying periods. It is in these reticulum and reticulo-endothelial lined spaces that the blood cells come in contact with the phagocytic white blood cells and histiocytes. Because of our repeated direct observations of pulp spaces in India ink injected spleens, we are convinced that the spleen circulation is peculiarly adapted to bring whole blood into contact with the reticulum pulp cells and thus provides most effectively for the arrest and phagocytosis of foreign particulate matter and of certain erythrocytes. The meshes of the pulp comprise a real, though rhythmically variable filter which separates blood cells from blood fluid. We believe it is probable that the hemolytic factors, other than, or in addition to, such as may be developed because of the mere physical dissociation of erythrocytes from plasma, are responsible for the excessive hemolysis that has been reported in splenic vein blood.

Fig. 7. Semidiagrammatic Drawing of Intermediary Circulation of Human Spleen

This drawing represents author's concept of architecture of reticulum and its relation to finest blood channels. Although it is not an actual reconstruction of serial sections, all structural details which are depicted in three dimensions have been observed histologically. For technical reasons, reticular fibers have not been drawn in different color but as ridges upon cytoplasmic syncytium. (From Klemperer, P.: Chapter on the spleen in Downey's "Handbook of Hematology." Paul B. Hoeber, New York, 1938, p. 1633. This and subsequent figures drawn from the same source are reproduced by kind permission of the publisher, Mr. Paul B. Hoeber.)

It is the presence of these pulp spaces and their probable function that should constantly be kept in mind in our discussion of certain of the splenopathies.

In considering the splenopathies it is

essential to remember that the spleen is not a unique organ but because of its mesenchymal origin in the primitive dorsal mesogastrium it is mesenchyme concentrated in the form of an organ closely associated with the portal vascular system. It, consequently, participates in the general reticulo-endothelial activities throughout the body. Splenomegaly, therefore, is not always a primary splenic disorder. It is our purpose to discuss only those splenopathies in which the intermediary circulation of the spleen, namely the terminal arterioles, the reticulum of the splenic pulp and the venous sinuses would seem to play a dominant rôle in the pathogenesis of the abnormal spleen and of the clinical picture.

CHRONIC HEREDITARY SPHEROCYTIC OR HEMOLYTIC JAUNDICE

The splenomegaly in this disease is explained by the microscopic picture which shows an enormous engorgement of the pulp spaces with red cells, with crowded, empty or collapsed venous sinuses, whose walls show slit shaped stigmata and narrowed lumina. The meshes of the reticulum are widely separated by the masses of red cells in the pulp spaces, but there also may be a hyperplasia of the lining reticulum cells of the pulp. Evidence of red cell phagocytosis and siderosis has not been found by many investigators using the older techniques. But the siderosis in the Kupfer cells in the liver and in the epithelium of the convoluted renal tubules in cases coming to autopsy, together with the constant finding of bilirubinemia and urobilinuria, is ample proof of the red cell destruction in this disease.

The explanation of the process of red cell destruction has not been satisfactory. That the factor of erythrolysis in the spleen, as an initiating if not the direct factor, is an important one is shown by the cure of the disease by splenectomy. Eppinger (10) has maintained that the engorgement of the reticular meshwork of the pulp creates conditions favorable to increased red cell destruction by reticulum cell phagocytosis. But what causes this astonishing engorgement of the spaces between the arterial capillary

Fig. 8. High Dry Photomicrograph (×530) of a Sinus Wall in a Section Stained with Phosphotungstic Acid Hematoxylin Combined with Silver-Ammonium Carbonate Impregnation.

(From Foot, N. C.: *Anat. Rec.*, **36**: 98, 1927. Reproduced by kind permission of The Wistar Institute of Anatomy and Biology.)

ampullae and the collapsed venous sinuses? Is it due to an arteriolar and capillary vaso-dilatation, as maintained by Klemperer (9), or to an inability of the spherical red cells to pass through the stigmata of the venous sinuses? The latter suggestion has not hitherto been made, but we present it as a possible explanation because of the evidence we

have seen in the study of the transilluminated venous sinuses.

The spherical erythrocyte is significant in this connection for two reasons.

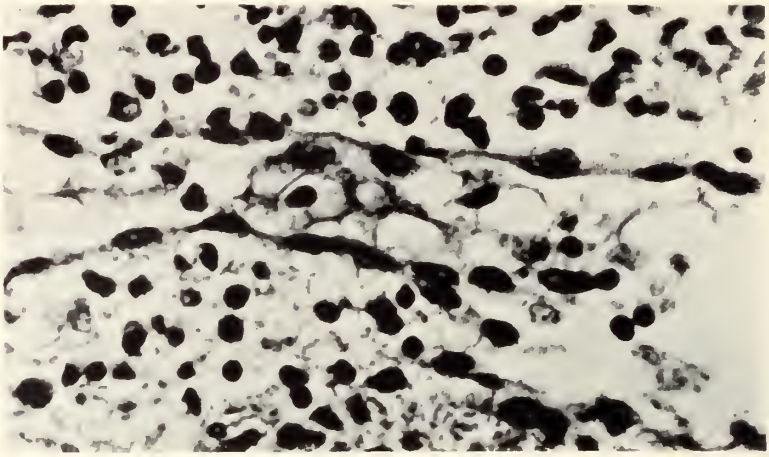

Fig. 9. Spleen of Calf. Structure of Sinus Wall

(From Klemperer, P.: Chapter on the spleen in Downey's "Handbook of Hematology." Paul B. Hoeber, New York, 1938, p. 1631.)

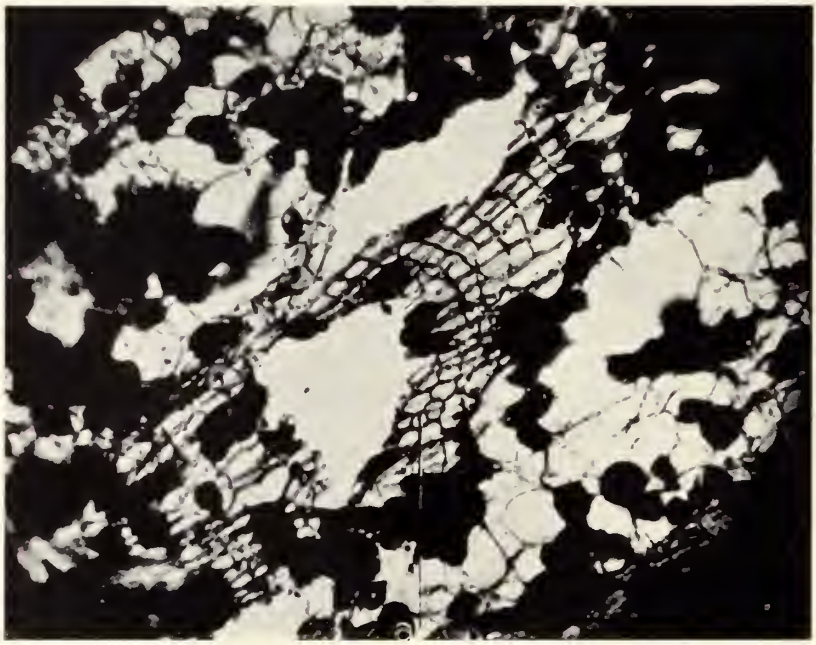

Fig. 10. Perfused Spleen of Dog

Sinus with circular and connecting longitudinal fibers (at *a*). Gelatine-frozen section, silver impregnation. Transverse cytoplasmic bridges are not well demonstrated because of overdistension of spleen by perfusion. (From Klemperer, P.: Chapter on the spleen in Downey's "Handbook of Hematology." Paul B. Hoeber, New York, 1938, p. 1629.)

First, it presents a greater general diameter than the normal biconcave red cell. This would seem to offer greater difficulty to passage through the slit-like stigmata of the venous sinuses. Secondly, the spherical red cell does not appear in rouleaux and is in a shape more susceptible to whatever hemolytic factor may be present in the pulp spaces of the spleen. Fåhraeus (11) has studied most thoroughly the rôle of the erythrocyte-plasma interface in relation to hemolysis and rouleaux formation. The presence of a lysolecithin in red cell destruction is one that must be considered in the massing of spherocytes in the pulp spaces either in primary erythrolysis in the spleen or as a preparatory phase for subsequent red cell destruction after the cells have escaped into the venous sinuses and from the splenic vein into the liver and other components of the reticuloendothelial system.

Additional evidence that a hemolysing factor is active in spherical red cell destruction in the pulp spaces is the finding by Orahovats (12) of increased red cell fragility to hypotonic salt solution in the blood that he aspirated from normal spleen pulp, and in the observation of Thompson (13), of our Spleen Clinic, that there is an enormous increase in spherical red cells in the pulp spaces in cases of hemolytic jaundice as compared to the numbers found in splenic vein blood in that disease.

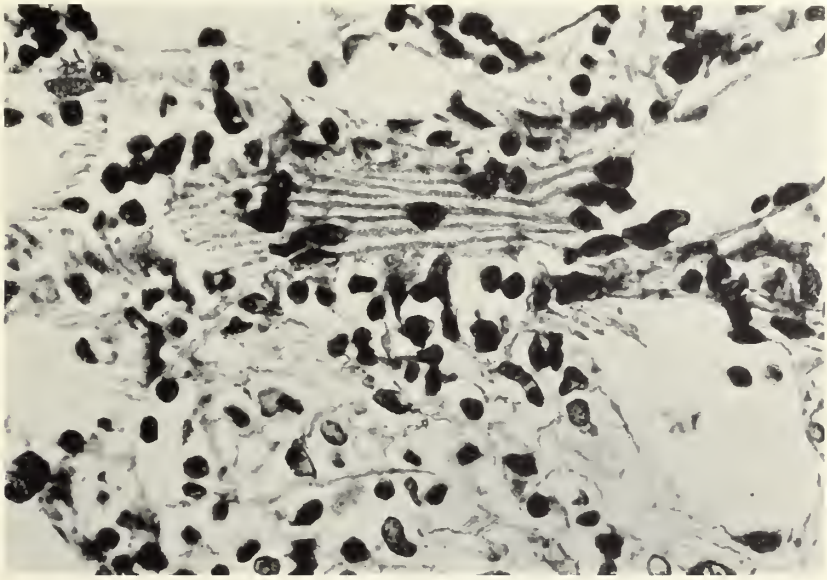

Fig. 11. Female Aged Twenty-Nine

Splenectomy for thrombocytopenic purpura. Perfused spleen. Tangential section of sinus. Heidenhain's iron hematoxylin. (From Klemperer, P.: Chapter on the spleen in Downey's "Handbook of Hematology." Paul B. Hoeber, New York, 1938, p. 1626.)

That there is in addition an active phagocytosis of red cells in the spleen is shown by MacKenzie's observation (5) which I quote: "In the course of observations on leukemic mouse spleens which, for the purpose of more clearly differentiating tumor cells from fixed and wandering phagocytes, had been subjected to (India) ink impregnation, we noticed that many of the macrophages revealed

clear ink free defects in their cytoplasm; some of them at the periphery, some deeper. Such defects bore no apparent relationship to the far larger nuclear structure. Their size approximated that of red cells, and at times, they transmitted light of a frankly pink or orange coloration. It seemed probable to us that these 'inclusion bodies' were recently phagocytosed erythrocytes, and we therefore attempted to repeat the finding in normal spleens with and without the assistance of ink. This we succeeded in doing to our ultimate satisfaction."

We wish to emphasize that the several evidences of red cell destruction definitely point to the pulp spaces, and not to the venous sinuses, as the area in which spherical red cells, especially, are brought in contact with the highly phagocytic, dynamic reticulum cells of mesenchymal origin. It is our belief that in individuals having the hereditary factor of spherical microcytes and red cells with an increased fragility, the intermediary circulation of the spleen is peculiarly adapted to the arrest of such red cells in direct contact with dynamic mesenchymal cells of the reticulum. The meshes of the pulp comprise an effective filter, rhythmically variable, which separates the blood cells from the blood fluid. It seems from our living-spleen studies that hemolytic factors, wherever elaborated in the spleen, are most active in red cell destruction during the phase of the circulation of blood through the intermediary pulp spaces, where because of their spherical shape these red cells pass with difficulty through the stigmata of the venous sinuses, become arrested in the pulp spaces and exposed for a longer time to a hemolyzing factor. This crowding of the pulp spaces in turn compresses the venous sinuses and narrows their stomata, setting up more or less of a vicious circle in the destruction of the red cells.

SPLENOMEGALY DUE TO PORTAL HYPERTENSION

The study of the circulation in the living mammalian spleen has interested us particularly in the relation of the intermediary circulation to the splenomegalies caused by portal hypertension, the result of obstructive factors in the portal bed. These splenomegalies are especially noticeable in the clinical picture spoken of as Banti's syndrome.

Banti (14) in 1883 first called attention to this syndrome and subsequently published ten more papers on the subject, maintaining that the hepato-splenomegaly was caused by some unknown toxic agent that first affected the spleen and subsequently the liver. He stressed the fact that the disease occurred more frequently in young individuals and more often in females, and that there was no association of this condition with antecedent disease of the stomach, liver or biliary tract, and that it was not associated with malaria, syphilis or alcoholism, that it was not hereditary, or limited to any definite locale. He described the disease as running a chronic course progressing in three stages: 1. The anemic phase with splenomegaly, asthenia and occasional gastrointestinal hemorrhages. 2. Transitional stage with oliguria, urobilinuria, hepatomegaly and brown discoloration of the skin and increasing gastrointestinal disturbances. 3. An ascitic stage with atrophy of the liver, subicteric sclerae, hemorrhages from the mucous membranes and death from hemorrhage or liver insufficiency. He noted the hematological findings of red cell pallor and a leukopenia with absolute or relative lymphocytosis. The pathology he described as present chiefly

in the spleen and liver with almost constant findings in the splenic and portal veins. The pathognomonic lesion he described as a conspicuous thickening of the fibrillar reticulum around the central arteries of the Malpighian corpuscles. "The fibroadenic alterations in the follicle distinguish the morbus Banti. Their absence rules out the disease." Progressive involvement of the follicles finally gave them the appearance of sclerotic nodules. He was unable to distinguish the liver pathology in the second and third phases from those seen in Laennec's cirrhosis.

Banti explained the pathogenesis of the disease as follows: An unknown, probably infectious, agent reaches the spleen by way of the arteries localizing in the follicular branches and causing the fibroadenia. Toxins elaborated in the spleen result in the general manifestations of anemia and asthenia, and the local lesions of endophlebitis of the splenic and portal veins, and cirrhosis of the liver.

In fairness to Banti it must be said that the term Banti's syndrome has not been confined to the entity as described by him. On the other hand, so few cases of hepato-splenomegaly with the anemia, leukopenia and gastrointestinal hemorrhages, as described by Banti, show the three stage progress of the disease that the term Banti's syndrome has replaced to a large extent the term Banti's disease. Inasmuch as Banti insisted that the fibroadenia of the follicles was the one pathological finding in the spleen essential to the diagnosis of morbus Banti, the finding of this fibroadenia in cases of splenomegaly, not fulfilling the clinical criteria of the disease described by him, and in cases with normal liver histology but with portal bed obstruction, invalidates the term Banti's disease.

Mennet (15) in 1920 and Dürr (16) in 1924 found intrafollicular periarterial fibrosis in cases of hepatic cirrhosis, portal bed thrombosis and ulcerative endocarditis. Klemperer (9) in his monograph on the spleen published in 1938 states that he has seen definite fibroadenia of the Malpighian corpuscles in thrombophlebitic splenomegaly and in cases of obliterated splenic and portal veins, in hepatic cirrhosis and in Cooley's anemia. Klemperer, whose views on splenic pathology are so authoritative, comments as follows: "Since the clinical picture is not characteristic and the histologic splenic lesions are not specific, a diagnosis in the early anemic period cannot be made with any degree of certainty. The alleged favorable results of splenectomy at this stage cannot be used as a basis for diagnosis of this disease, because there is no evidence to prove that the progress of the disease was actually arrested. An improvement in the late cirrhotic stage also does not help to identify such cases because similar successful results after splenectomy have been reported in undoubted 'primary' liver cirrhosis. The hematologic findings are certainly not pathognomonic, since anemia and leukopenia have been observed in many splenomegalic conditions as well as in atrophic cirrhosis (Naegeli (17) 1931). From the foregoing considerations it becomes apparent that the clinical symptoms likewise do not justify the recognition of Banti's disease as a distinct morbid entity. Because of the foregoing clinical and pathologic considerations, the diagnosis 'Banti's disease' should be abandoned."

The members of our Spleen Clinic at the Columbia-Presbyterian Hospital have for a number of years been especially interested in this syndrome of splenomegaly with anemia, leukopenia and thrombocytopenia, associated with the

development of increased collateral circulation between the portal and peripheral venous systems and characteristic histologic changes in the spleen. The patient who first demonstrated to us this syndrome in complete conflict with Banti's hypothesis was a young, vigorous policeman giving the following history: In 1928, in attempting to stop a runaway team he was pinned between an elevator pillar and the tongue of the wagon. This resulted in a rupture of the pancreas, for which he was operated upon at the Post-Graduate Hospital by Dr. John Erdman. A few months later he developed a pancreatic cyst which Dr. Erdman removed. At this time his spleen was not enlarged and his blood picture was normal. During the next three years he gradually developed a splenomegaly and an anemia with a leukopenia and thrombocytopenia and had two severe hematemeses. The clinical picture and diagnosis of Banti's syndrome was evident. In 1932 I removed his spleen, finding at that operation a very large spleen with enormously dilated splenic vein, which entered dense scar tissue at the site of the injury to the pancreas, resulting in splenic vein obstruction and diffuse collateral circulation between the splenic vein and branches of the left gastric and left gastro-epiploic veins. The liver appeared normal in every respect. This patient made an uneventful recovery and his blood values promptly returned to normal and remained so for the next nine years of his follow-up. He had no recurrence of hematemesis.

This finding of a normal liver on the right and a splenomegaly on the left with an obstructive factor between and the picture of Banti's syndrome initiated certain studies which have clarified our ideas regarding the pathogenesis of what we agree with Larrabee (18) should be called congestive splenomegaly.

Our Spleen Clinic studies on splenic vein pressures made at the time of splenectomy and compared with peripheral venous pressures were reported by us in 1937 (19). These showed an increase of two to five times splenic vein pressure over peripheral venous pressure in cases presenting Banti's syndrome. Table I shows the comparative readings in the different types of splenomegaly.

It is our present concept that Banti's syndrome is the result of mechanical obstruction to the flow of blood within the portal bed. Thompson (20) has recently published the views of our clinic. They may be summarized as follows:

The site and character of this obstruction must be such that a gradually progressive increase in portal bed pressure will develop, with the peripheral venous pressure remaining normal. This gradual increase in portal vein over peripheral vein pressure with the absence of valves in the portal vein, results in the development of collateral branches and the maintained engorgement of the spleen and is the actual cause of the splenomegaly. The site of the obstructive factor in the portal bed determines the extent and the distribution of the collateral circulation and the volume of the reversed blood flow. The obstructive lesions in the portal bed may be divided, from the standpoint of gross pathological findings at operation or at autopsy, into two main groups: intra-hepatic and extra-hepatic. The intra-hepatic lesion responsible for congestive splenomegaly is some form of cirrhosis. In some 140 cases studied in the Clinic, cirrhosis was present as the obstructive factor in 68 per cent.

Of special importance is the relation

between the type of hepatic scarring and the degree of portal hypertension. Cirrhosis in general is associated with more or less congestive splenomegaly. It is very important to determine what types of cirrhosis result in congestive splenomegaly and what types do not.

over a long time, resulting in a slow but progressive rise in portal vein pressure. Secondary to this portal hypertension there develops the splenomegaly and the rest of the syndrome of Banti. Rousselot and Thompson (21) have reproduced this picture experimentally by injecting

TABLE I

Venous Pressures in Millimeters of Normal Saline

Pt.	Splenic Vein	Arm Vein
Banti—Laennec Cirrhosis		
C. M.	225	12
C. M.	325	85
D. P.	450	125
N. A.	470	145
R. B.	370	30
S. S.	360	150
G. A.	260	190
Banti—Thrombosis of Splenic Vein		
J. S.	390	170
Banti—Schistosomiasis Mansoni		
P. R.	250	50
A. E.	335	105
G. P.	500+	70
C. C.	415	125
L. M.	375	60
H. B.	377	110
Banti—Obstructive Factor Undetermined		
L. D.	275	105
C. K.	370	50
B. S.	330	55
P. M.	465	110

Controls			
Pt.	Splenic Vein	Arm Vein	Diagnosis
F. H.	190	65	Lymphosarcoma
R. B.	105	80	Hemolytic jaundice
L. L.	220	205	Atypical hemolytic jaundice
N. B.	125	130	Hemolytic jaundice
S. S.	215	40	(shock) Gaucher's
L. L.	190	107	Splenomegaly of undetermined origin
W. U.	120	95	Hemolytic jaundice
S. J.	360	−5	(severe shock) Purpura
Z. G.	185	75	(beginning shock) Pancreatic adenoma
S. L.	190	210	Purpura
G. C.	235	165	Splenomegaly of undetermined origin
E. N.	275	205	Atypical hemolytic jaundice
T. K.	70	300	Purpura
M. M.	140	65	Purpura
J. K.	245	240	Lymphatic leukemia
A. M.	175	125	Splenomegaly of undetermined origin
J. B.	225	185	Hemolytic jaundice
H. A.	180	20	(in shock) Reticulo-endotheliosis
H. R.	290	290	Giant foll. hyperplasia
S. R.	180	165	Hemolytic jaundice

1. The type of liver scarring that is seen in late cases of schistosomiasis Mansoni results in the greatest increase in portal bed pressures and the largest spleens. The presence of fragmented ova of this parasite in the smaller intra-hepatic portal radicals causes the typical "pipe stem" type of peri-portal scarring

finely divided silica particles into the splenic vein of dogs. After two years a very large spleen develops with very extensive collateral circulation and esophageal varices.

2. In our experience biliary and cardiac cirrhosis do not produce splenomegaly. Very rarely, prolonged cardiac decom-

pensation may result in peri-portal scarring and splenomegaly.

3. Laennec's cirrhosis is associated with a variable degree of splenomegaly, depending upon the amount of peri-portal scarring. This is seen in 60 per cent of the 81 cases studied by Thompson (20) in the Department of Pathology of Columbia University. In the remaining 40 per cent there is less connective tissue in the peri-portal area and more injury to the liver parenchyma. These patients usually die of hepatic insufficiency in cholemia; the former group are more often terminated by esophageal hemorrhages.

4. In the splenomegalies due to extra-hepatic obstructive factors, the lesion is due to traumatic or inflammatory scarring of some part of the portal bed or to such a lesion as cavernomatous transformation of the portal vein. In the children developing the Banti syndrome in infancy we have wondered if the portal vein block might not be due to a congenital defect in the vein or to a thrombosis of the portal vein as a continuation of the normal thrombosis of the umbilical vein. Rousselot (22) has recently reported on four of our younger extra-hepatic group showing a stenosis of the portal vein. We believe that this lesion is responsible for this noncirrhotic group of Banti's syndrome occurring in infancy and childhood.

5. If at the time of splenectomy the congestive splenomegaly is associated with a normal liver, as demonstrated by liver biopsy, cirrhosis will not appear subsequently. We have followed many such extra-hepatic portal bed obstructions for long periods in our follow-up or to autopsy without finding a subsequent cirrhosis.

6. The therapeutic effect of splenectomy, as regards subsequent hematemesis, depends upon the site in the portal bed of the obstructive factor. Unfortunately, only a small percentage of these splenomegalies are due to splenic vein obstruction. These cases are cured by splenectomy. In the other cases of extra-hepatic portal block and in the intra-hepatic group, the portal hypertension results sooner or, sometimes years, later in recurring gastrointestinal hemorrhage.

Bear in mind the anatomy of the intermediary circulation in considering the pathology of chronic portal bed obstruction. The most characteristic feature in the microscopic sections of these splenomegalies is the widening and distention of the venous sinuses with a widening of the stomata resulting in a compression of the splenic pulp spaces. In addition, there is a hyperplasia of the cytoplasmic reticulum. The back pressure in the venous sinuses, transmitted by the hypertension in the veins, causes the distention of the venous sinuses and the narrowing of the pulp spaces. This makes it more difficult for the blood to pass from the arterial capillaries into the pulp spaces. This results in hemorrhages about the trabecular arteries and at the periphery of the follicles, with a later development of nodular areas of fibrosis—the typical fibroadenia described by Banti.

This more or less exclusion of the splenic pulp from active circulation results in a gradual atrophy of the reticulum with connective tissue replacement and a fibrous spleen. The gradually increasing portal hypertension which Rousselot and Thompson (21) produced in dogs' spleens by the injection of silica particles into the portal bed resulted in the same type of splenomegaly, both in the gross and in microscopic section, that one sees clinically in patients with Banti's syndrome. These dogs develop a marked

portal hypertension, an anemia and a thrombocytopenia. These experiments together with the finding in an increasing proportion of the obstructive factor in the portal bed in clinical cases convince us that splenomegaly in Banti's syndrome is the result of portal bed hypertension, and that the intermediary circulation as seen in the living mammalian spleen correlates the pathological changes found in the splenomegaly caused by portal hypertension.

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The Problem of Epidemic Influenza*

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THE fundamental problem confronting the student of epidemic influenza is primarily that of explaining its numerous recurrences. In the course of its history all variations of disease from the mildest indisposition to the most rapidly fatal pneumonias, from outbreaks of acute intestinal disorder to chronic, slowly progressing encephalitis have been attributed to influenza. This confusion in diagnosis has prevailed despite the fact that the symptomatology of epidemic influenza has for centuries presented an amazing uniformity. The disease is characteristically epidemic; it develops quickly, spreads rapidly to as much as 30 to 50 per cent of the population, although fatal to few, and terminates abruptly. Within a short period of years it reappears in the same geographical area. The clinical picture and the epidemiological features are then repeated with little modification except for variations in extent, in severity and in the incidence of complications. The very frequency of the recurrences in adult populations has been sufficient to indicate that epidemic influenza differs immunologically from many of the common infectious diseases; that either immunity is of brief duration or that serologically divergent strains of virus are disseminated in different outbreaks and that the strains vary in virulence and infectivity. These suggestions were originally derived from broad epidemiological considerations, but since the isolation of influenza virus in 1933 by Smith, Andrewes and Laidlaw (1), studies of the strains of virus involved in six epidemics have yielded a significant body of information.

I shall attempt in the course of this presentation to survey the knowledge of variation in virus strains and its application to the problem of recurrent epidemic influenza. Since it has been my good fortune to have participated in certain of these studies, I shall ask your permission to draw to a great extent upon the evidence with which I am personally familiar.

BASIC STUDIES

From 1933 to 1936 studies in various laboratories were mainly concerned with the isolation of virus in epidemic areas and the establishment by immunological means of the identity of the virus involved (2, 3, 4, 5, 6, 7). Mice were found to be susceptible and the scope of experimental studies was thereby extended greatly (2, 8). By means of the neutralization test in mice it was shown that antibodies to the virus were common in the serum of human individuals of all ages, excepting young children (3, 9, 10). The virus of swine influenza was shown to be serologically related to, although distinguishable from, the strains of human influenza virus (1, 4, 11, 12, 13, 14). A diagnostic test, in addition to isolation of virus, was found to be available in the demonstration that a sharp rise in antibodies neu-

* James M. Anders Lecture XVI, The College of Physicians of Philadelphia, January 8, 1941.

tralizing influenza virus occurred in the serum of patients convalescent from the disease (4, 7, 15, 16). This increase in antibody titer was detectable by a comparison of the titer of serum taken during the acute phase of illness with that of the convalescent serum. Subsequently, the complement fixation reaction was found to yield comparable results when the patient's serum was tested against an antigen prepared from virus-infected tissue (15, 17). The ground work was thus laid for intensive study of subsequent epidemics.

Since January, 1936, four epidemics have occurred. The studies conducted during these periods have yielded interesting contrasts. That of the winter of 1936–37 extended over the entire northern hemisphere. Virus was isolated in numerous laboratories in the United States, Europe and the Far East. When throat washings from individual patients were examined the virus was demonstrated in as high as 80 per cent of the cases (15, 16, 18). Strains of virus infected ferrets readily and for the first time the infection was transmitted directly from man to mouse (19). The serological reactions were firmly established to be valuable not only as confirmatory evidence of virus infection but also in the diagnosis of clinical cases from whom virus was not recovered, and in the recognition of subclinical infections. This outbreak constituted, then, a pandemic of undoubted etiology due to virus of relatively high pathogenicity.

In 1938–39 epidemic influenza was detected in the United States (20, 25), England (21), Holland (22) and Australia (23, 24). Most of the reports are of extremely mild institutional occurrences. Virus was isolated in only 10 to 20 per cent of trials and the strains were of low virulence for ferrets and mice. The incidence of the disease in the general population, as represented by our studies (25) at Bellevue Hospital, was low. Nevertheless, in the institutional outbreaks reported by Horsfall, Hahn and Rickard (20), and by Burnet (24), that the incidence of the disease was high was shown by the large proportion of positive serological reactions. The mildness of this epidemic was in sharp contradistinction to that of 1936–37, although the evidence indicates that the lack of severity did not prevent its wide dispersion. The results suggest that the difference in severity of these two outbreaks was indeed related to a difference in the virulence of the strains of virus involved.

SEROLOGICAL DIFFERENCES IN STRAINS OF INFLUENZA VIRUS A

The strains of virus isolated from the epidemics of influenza of 1932–33, 1934–35, 1936–37, and 1938–39 have all been identified as specimens of the same virus. On the basis of early serological studies, they appeared to be identical. The serum of a ferret recovered from infection with one strain neutralized other strains; mice vaccinated with one strain were immune to others; rabbits vaccinated repeatedly with one strain produced antibodies which neutralized others; the rise in antibodies in the serum of patients recovering from infection during any of these epidemics was measurable by tests conducted with any of the standard strains such as WS or PR8. This seemed convincing evidence. Nevertheless in 1936, Magill and I (26) demonstrated that serological differences between strains of this virus did exist and charted the differences and similarities of 24 such strains (27, 28). For this purpose neutralization tests with serum of rabbits taken early in the stage of

antibody response to vaccination were used. Additional evidence was obtained by cross testing the active immunity of vaccinated mice to infection with homologous and heterologous strains of virus. On this basis the strains from any single epidemic appeared to be more closely related to one another than to strains from other epidemics. Nevertheless, the entire picture represents a spectrum of antigenic structure in which the different strains are made up of varying proportions of similar components rather than being sharply divided into groups of strains of unrelated composition. These studies have been substantiated by Smith and Andrewes (16, 29), by Burnet (24, 30) and others.

Serological variations of this degree require consideration in the problem of specific vaccination. There is considerable disparity in the capacity of any single strain to immunize mice against other strains of the same virus. Nevertheless, the effect is to a great extent dependent upon the intensity of vaccination, since repeated inoculations will eliminate strain specificity. And, as was originally demonstrated by Shope (12), and Francis and Magill (4), the base of resistance may be so broad under these conditions as to give cross immunity between strains of swine and human origin. The significance of these differences as factors in the recurrence of epidemics is not yet established. However, Horsfall and Lennette (31) have demonstrated that in the ferret, infection with one strain may not give rise to active immunity against another strain of relatively different antigenic structure. Magill and Sugg (32) have reported that the serum of a given individual may vary in titer when tested against similar strengths of different strains of virus, but that following infection with still another strain, the antibody titer rises against all. Horsfall (33) has also observed that the increase in neutralizing antibodies following infection is independent of the strain of virus used for testing, substantiating results obtained by other workers, using a standard strain for serological diagnosis. Furthermore, complement fixation tests reveal that the participating antigen is common to all strains and even fails to distinguish between strains of porcine and human origin. To summarize: strains of the same virus can be differentiated serologically; they are, nevertheless, closely related through possession of common antigens. Diagnostic tests with one strain appear capable of detecting infection with another. Strains from the same epidemic tend to exhibit similar serological features. Immunization with one strain may not, under certain conditions, give rise to complete immunity to all strains. Whether these serological variations are sufficiently great that one strain may become epidemic in a human population immune to another is not yet known.

The disease caused by this virus appears to be an etiological entity identified through the immunological relationships of the associated virus strains and the common serological reactions of patients in different epidemics where the virus has been encountered. The etiological and epidemiological evidence derived from investigations of the four epidemics of alternate years is very precise. It has taken from the great mass of respiratory disease one epidemic infection and characterized it on an etiological basis which is entirely independent of clinical severity. The disease and its accompanying virus have been widely dispersed in at least three of the epidemics despite pronounced differences in intensity. It has been recently suggested (34) that the

term, Influenza A, be applied for identification of this disease caused by strains of the forementioned virus derived from human sources.

INFLUENZA B

While progress in the delineation of the disease, epidemic influenza, was notable, certain gaps in the picture had become quite prominent. The first of these concerned a widespread epidemic of influenza occurring in the early months of 1936 (35). The epidemic was originally recognized in California, where by house to house canvasses in different communities it was ascertained that 35 to 40 per cent of the population was attacked. Although individuals below the age of 20 constituted about one-third of the population, the percentage of cases occurring in this age group was nearly 50 per cent. In some communities 60 per cent or more of the population in the ages of 5 to 19 were affected. The epidemics rose abruptly and subsided rapidly. The illness as observed appeared to be typical of epidemic influenza; the onset was sudden, with chills and fever, headache, generalized aches and pains, nasal and pharyngeal irritation without evident coryza. In most instances the fever was of 3 days' duration. Hoarseness and cough began not infrequently at the time the temperature reached normal and persisted for an indefinite period. In a small proportion of cases bronchitis or bronchopneumonia developed. Physical examination usually revealed little except a flushed face and a dry pharynx with swollen lymphoid follicles but without exudate. Temperatures ranged up to 104°F. Muscular tenderness was frequently evident. Convalescence was commonly associated with a protracted weakness and depression. The leukocyte count in 73 per cent of cases was less than 7,000 per cu. mm.

Efforts to isolate epidemic influenza virus from throat washings of 33 patients were unsuccessful. Furthermore, neutralization tests done with acute and convalescent sera of these patients against the standard PR8 strain of Type A virus failed to reveal an increase in antibodies during convalescence. The disease spread throughout the greater part of the United States, but the results of studies made in numerous communities were equally disconcerting. We were left with an epidemic of influenza, typical clinically and epidemiologically, which gave no intimation of relationship to Influenza A. The only reasonable conclusion was that the epidemic had been caused by an entirely different virus.

Four years later the same experience was had. In January, 1940, epidemic influenza appeared in the southeastern portion of the United States. The number of cases is unknown, but in North and South Carolina alone figures indicate that several hundred thousand people were affected, since over 16,000 cases were actually reported from South Carolina in a 5 week period. Although our studies included material from only 7 patients, the results of neutralization and complement fixation tests done with the patients' sera against the PR8 strain of virus were completely negative. In some instances, ferrets inoculated with throat washings of the patients developed febrile reactions but when serial passages were made in other ferrets the evidence of infection was so slight as to discourage additional passage. Furthermore, the convalescent ferrets' sera failed to neutralize standard influenza virus. Horsfall (33) reported similarly negative results in a larger series of experiments.

At this time a mild epidemic of acute

respiratory disease was encountered by Reyersbach, Lenert and Kuttner (36) at Irvington House, a sanatorium for rheumatic children. In a period of 30 days, 50 of 108 children took sick. The illness was differentiated clinically from an outbreak of pharyngitis due to streptococcus hemolyticus which had been in progress by the absence of sore throat, the predominance of constitutional symptoms and by a characteristic leukopenia at onset. Dr. Kuttner made material from typical early cases available for study. All diagnostic tests conducted with the PR8 strain of Influenza A virus were negative. After prolonged passage in ferrets and mice, a virus was isolated from the throat washings of one patient (Lee) (37). This virus of low virulence was not neutralized by sera prepared against a large variety of strains of Type A influenza virus or by serum against swine influenza virus. It was neutralized, however, by serum of a convalescent ferret employed in the passage series before adaptation to mice had been begun. When the acute and convalescent sera of patients who had been ill during the outbreak at Irvington House were tested against the new virus, sharp rises in titer of the convalescent sera were demonstrable, although the same sera had failed to show the characteristic rise in antibodies to known influenza virus. These results indicated clearly that the new virus was etiologically related to the epidemic of influenza at Irvington House and that the virus was quite different serologically from strains of influenza virus previously isolated in epidemic periods.

The serum of patients from North Carolina and of ferrets which had received their throat washings were then retested with the new virus. Here again sharp increases in neutralization titers of the convalescent sera were demonstrable. Additional sera from other patients in the North Carolina epidemic and of inoculated ferrets had been found by Dr. F. L. Horsfall, Jr., to be entirely negative when tested against Type A influenza virus. Certain of them were then titrated against the recently isolated virus with positive results. The causal virus of the extensive epidemic of the Southeast in January and February of 1940 was thus identified. In a similar manner sera from ferrets and human individuals revealed that the new virus was involved in the epidemic in Cuba during the summer of 1940.

From these studies had evolved the isolation of a new strain of virus which was dominantly responsible for the epidemic influenza of the early months of 1940 and also participated in the summer epidemic in the West Indies. They led to the recognition that the virus was different serologically from known influenza virus as shown by the fact that the antibody response of convalescent patients or ferrets was detected only by serological examinations conducted with the homologous virus. Through these observations a widespread epidemic disease of 1940, indistinguishable from epidemic influenza of Type A, was transferred from the group of unidentified respiratory infections to a position of recognized etiology. For purposes of identification it has been designated Influenza B.

The next step was to investigate the relation of the newly identified agent to epidemics of other years. It has already been mentioned that from a high proportion of cases studied during the epidemic of the winter of 1936–37, virus of Type A had been recovered. Similarly, serological tests with the serum of patients and virus of Type A had been regularly

positive. Acute and convalescent sera from nine patients of that epidemic were in storage. They were retested against virus of both Type A and Type B. All showed the typical increase in antibodies to the PR8 strain of Type A, but none was positive to Type B virus. Thus, as all previous evidence had indicated, the 1936–37 epidemic was not associated with virus of Type B.

With acute and convalescent sera which had been obtained in 1938–39, six showed sharp rises against Type A virus but not against Type B, five showed no response to either virus, while two revealed an increase in antibodies to Type B but not to Type A. Although these cases represented individuals selected from a large number as most closely resembling influenza, the clinical variation was great. Nevertheless, the evidence suggests that in addition to the greater prevalence of Influenza A in 1938–39, Influenza B had also been present in the community.

The epidemic of the early months of 1936, which had remained of undetermined etiology (35), was again investigated by testing the stored acute and convalescent sera of 30 patients against the PR8 strain of influenza virus, Type A, and against the Lee strain of influenza virus, Type B. In 23 instances pronounced increases in antibody to the new Type B virus but not to Type A were demonstrated; in five, no increase in antibodies to either virus occurred, while in two, the convalescent titer was definitely increased against both. There was little doubt, therefore, that this widespread epidemic, the cause of which had eluded us four years earlier, was attributable to Type B influenza virus. The establishment of this fact was of extreme significance since it indicated that the new virus was not an aberrant type which had suddenly arisen, but rather that it had previously occupied a definite place in the history of epidemic influenza.

RELATIONSHIP OF INFLUENZA A AND INFLUENZA B

One can seriously question whether cross immunity obtains between Influenza A and Influenza B. In the first place, a relatively large percentage of the cases observed had, at the time of their infection with Influenza B, titers of neutralizing antibody to Influenza A of such height as to indicate that they were resistant to Influenza A. At the same time their antibody titers to Influenza B were extremely low. As the titer of antibodies to Influenza B virus rose in convalescence, those to Influenza A virus remained unchanged. The reverse was also true; infection with strains of Type A virus resulted in an increase of antibodies to the homologous virus but not to that of Influenza B. Hence, the production of neutralizing antibodies appears to be quite specific for the type of virus involved.

TABLE I

The identification of type of virus infection in epidemics of influenza

Epidemic	No. of cases	Neutralization tests with patients' sera			
		A + B −	A − B +	A − B −	A + B +
1940					
Irvington	8	0	7	1	0
No. Carolina	11	0	10	1	0
Cuba	3	1	2	0	0
1938–39	13	6	2	5	0
1936–37	9	9	0	0	0
1936	30	0	23	5	2

As measured by the complement fixation reaction, infection with one strain of Influenza A virus gives rise to antibodies

which react uniformly with all strains of that virus and with swine influenza virus. In a limited number of tests it has been observed that complement-fixing antibodies acquired in convalescence from Influenza B react only with Type B antigen, not with Type A antigen—and vice versa (38). Thus, the reactive component, common to strains of Type A virus, is missing in the Type B virus, a fact which emphasizes again the serological specificity of Type B virus.

Hyperimmune serum prepared by repeated inoculation of ferrets or rabbits with the PR8 strain of Influenza A virus has failed to exert any neutralizing effect upon the Lee strain of Type B. Nor has any of a large number of immune swine sera shown evidence of neutralizing it. Furthermore, vaccination of mice with 3 doses of Influenza A virus, which results in homologous immunity sufficient to protect the animals against one million intranasal lethal doses, has given no immunity against a single fatal dose of the Type B virus. Similarly, mice vaccinated with the Type B virus are fully resistant to maximal infectious doses of the same agent but exhibit no immunity to Type A virus.

In consequence of these data, there is at the moment little immunological evi-

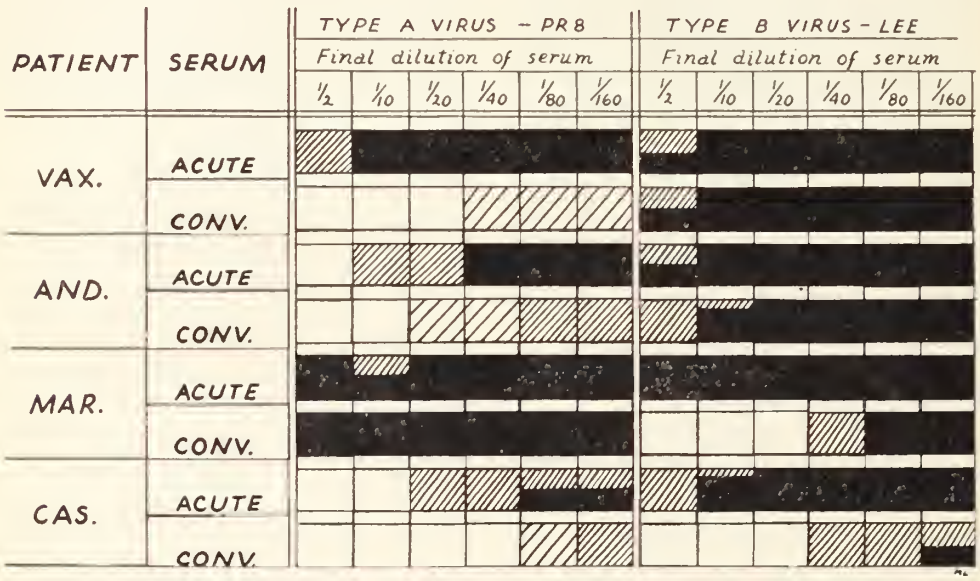

CHART I

dence that the two diseases are in any manner related. Clinically and epidemiologically, however, no clear differences between them have been detected, although future studies may reveal distinctive features. In mice, Type B virus produces a disease which closely resembles that resulting from infections

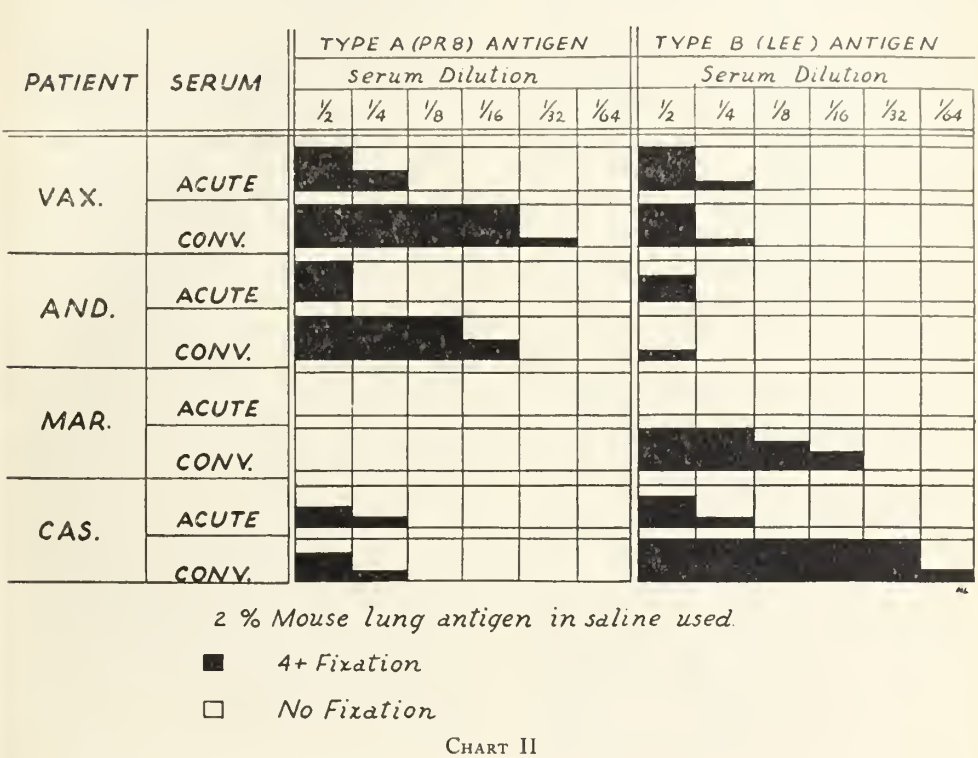

CHART II

TABLE II

Lack of cross immunity in mice vaccinated with influenza virus, Types A (PR8) and B (Lee)

Vaccination i.p.	Infection i.n.	Size of infecting dose of virus						
		10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}
3×10^{-3} PR8	PR8	± 0 0 0 0	0 0 0 0 0	± ± 0 0 0				
	Lee	5 6 6 6 6	6 6 7 7 +++	5 7 9 +++ ++				
$3 \times 5\%$ Lee	PR8			3 3 3 4 4	3 3 4 4 5	2 3 7 ++ ++		
	Lee	0 0 0 0	++ 0 0 0	0 0 0 0				
Controls	PR8					5 5 5	7 7 8	7 +++ ++
	Lee		7 7 7	7 9 10	++ ++ +			

Numerals = days of death of individual mice.
0 = mouse survived 10 days without pulmonary lesions.
± to ++++ = increasing degrees of pulmonary lesions at autopsy on 10th day.

with virus of Type A. In ferrets the disease has not been greatly different from that produced by mild strains of Influenza A virus. Since the diseases in nature and in experimental animals resemble one another in many details, it appears desirable for the present, at least, to retain the term, Influenza B. The 2 large outbreaks of Influenza B in 1936 and 1940 began in the early months of the year, while the tendency of the 4 epidemics of Influenza A in alternate years since 1932–33 has been to gain momentum in November or December. One might suggest, therefore, that Influenza A recurs biennially while Influenza B is a quadrennial croup. In any case, the two diseases appear to travel independently, although indications exist that they may occur simultaneously or continuously.

One other point, I should like to mention briefly. In 1936 an entirely different virus was encountered and repeatedly isolated (39). One can only say that this virus was recovered from ferrets which had received throat washings of patients at that time. Its identity was not established, although certain suggestions were made and it was tentatively designated meningo-pneumonitis virus. Recently, Eaton, Beck and Pearson (40) have reported that the virus is immunologically related to psittacosis, a possibility we had discussed but tended to dismiss. They have also found a similar strain of virus in cases of virus pneumonia. One immediately is confronted again with the possible relation of this virus to the epidemic of 1936. It has been my belief that the virus at that time was resident in the ferrets and was enhanced by passage. The demonstration of the serological responses of these same patients to the new Influenza B virus tends to substantiate this belief, since the Influenza B and the meningo-pneumonitis viruses are quite dissimilar.

It is apparent that in this discussion I have failed to present many aspects of the problem of epidemic influenza: the important rôle of bacterial agents in enhancing the severity of the disease; the continuous migration versus resident host concept; the duration and the mechanism of immunity; specific prophylaxis and many other features. Nevertheless, it seems to me that an understanding of most of these questions has its basis in a clear evaluation of the agent involved in recurrent outbreaks. It has been seen that variations in the clinical severity of the disease have been associated with quantitative differences in the pathogenicity of the associated strains of virus; that within the confines of what has been called Influenza A significant immunological differences in the strains of that virus occur. Moreover, at least two widespread epidemics of influenza have been found to be caused by a virus which is sufficiently distinct serologically as to indicate that it is an entirely different virus. It is obvious, therefore, that there are fundamental differences in the causative agents of epidemic recurrences and that these differences are of primary significance for an understanding of immunity and the development of prophylactic measures.

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The Penetration of Pathological Anatomy in the First Half of the Sixteenth Century as Illustrated by the *Medicina* of Jean Fernel*

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ANATOMICAL localization is part of the concept of disease. The progress of medical science has consisted in large measure of increasingly close correlation of functional disorder and organic abnormality. For a fair view of the prevailing medical understanding of any period one turns to the most influential texts of the time, for such books are the products of current thought and mould the concepts of a limited number of years to come. And so we may examine the most authoritative compendia of medicine of any early period for a comparative picture of the state of advancement of anatomical penetration in medical thought at the time.

The *Medicina* of Jean Fernel was one of the most widely read text books of general medicine in the sixteenth and seventeenth centuries. First published in 1554, it passed through some thirty editions, reprintings and partial translations. Its author was one of the most respected scientists in France, a mathematician and astronomer, as well as a physician, a man of letters noted for his wide reading and scholarship, and physician at the royal court. An enthusiast of a later century, Bordeu, placed him on a par with Celsus and Avicenna, almost on a plane with Galen, and but little below Asclepiades and Hippocrates. His *Medicina* was wide in scope, intended to cover medicine *in toto*, as its title indicates, and, it would seem, might well be examined for the current state of any of the medical branches.

THE LIFE OF FERNEL

Before we do this, however, it may be of interest briefly to review the life of Fernel himself. Unfortunately its beginnings are not well known. The date of his birth is uncertain. His leading pupil, Guillaume Plancy (Plantius, Plancius, Planche, etc.), in a biography presumably written shortly after Fernel's death, but not published until 1607, stated that Fernel was seventy-two years old when he died, "in the year of Christ 1557." This seemingly would place his birth in 1485, but it is known that the date 1557 resulted from a peculiar method of reckoning time, and that Fernel died in 1558, so that if the age of 72 years is correct the date of birth was 1486. Fernel was buried in the Church of Saint Jacques. In his epitaph on a copper tablet set in the wall near the tomb occurs the line *obiit 26 Aprillis anno MDLVIII. Vixit annos LII.* This implies that he

* Presented before the History of Science Society, Columbus, Ohio, December 29, 1939, and scheduled for publication in *Isis*, the official organ of that Society. As the date of publication in *Isis* is indefinite, owing to difficulties created by the war, the editor, Dr. George Sarton, has kindly given the author permission to publish the paper in the *Transactions & Studies*.

was born in 1506. It has been maintained, however, that the tablet erred through the omission of two letters and that LXXII was intended. The subject is exhaustively discussed in Eloy's *Dictionnaire historique de la médecine ancienne et moderne* (Mons, 1778), with notation of the views of the many biographers who took part in the dispute. The place of Fernel's birth is also uncertain. It was given as Clermont by Plancy and Mondidier by others.

It appears to be certain, however, that he went to Paris to complete his education and studied at the college of Sainte Barbe. He became an ardent student of mathematics and philosophy, and is said to have devoted himself to his studies with such intensity that his health failed. Something more definite than the effects of mere work ailed him, however, for we read that he suffered from a serious "quartan fever," to recover from which he retired from Paris to the country. Ac-

ΙΛΕΡΜΟΣ Ο ΠΛΑΓΚΙΟΣ ΕΣ ΤΟΝ
ΛΑΜΠΡΟΤΑΤΟΝ ΦΕΡΝΕΛΙΟΝ.

Πως τε τὰ σώματ' ἔχει φύσει, ἠδ' ἐς νοῦσον ὀλισθεῖ,
Εργον τ' ἰητροῦ, κάλλιον οὔτις ἐρεῖ.

Fig. 1. Portrait of Jean Fernel. Below it is a Complimentary Couplet to Fernel from his Pupil, Biographer, and Commentator, Guillaume Plancy.

IO. FERNELII
AMBIANI,
Medicina.

AD HENRICVM .II. GALLIARVM
REGEM CHRISTIANISSIMVM.

LVTETIÆ PARISIORVM,

APVD ANDREAM WECHELVM, SVB
PEGASO, IN VICO BELLOVACO.

1 5 5 4.

Cum Priuilegio Regis.

Fig. 2. Title-Page of the First Edition of Fernel's 'Medicina'.

cording to Plancy, the illness led him to devote himself to the science of medicine, although when he returned to Paris, it was not to take up this discipline exclusively; his original interest in mathematics continued to hold his chief attention, and absorbed most of his income as well. It was indeed the mounting cost of his instruments and apparatus that finally led him to devote himself to a profession yielding more financial return. About 1535, five years after he received his doctorate, he began the practice of medicine.

Success as a physician came rapidly, and in the succeeding years of his life he acquired great reputation and amassed a fortune. His patients included the king's favorite, Diane de Poitiers, and it took considerable resolution on Fernel's part to escape for some time the arduous position of physician to the king himself. At least twice he refused Henry the Second's invitation, in order to remain at the scholarly labors he preferred, feigning illness the first time, and refusing on the second occasion on the ground that he did not wish to supplant as distinguished a man as Louis de Bourges, who had held the position at court since the days of Francis the First. In 1556, however, when Louis died, he no longer had an excuse, and in this year he accepted Henry's repeated invitation. It was close to the end of life for each. In the severe winter of 1558 Fernel's wife died at Fontainebleau, and Fernel, himself, profoundly saddened, followed her within a few weeks. A necropsy was performed, which will be described later.

As physician in the king's household he attended the queen, Catherine de Medici. Her extraordinary fertility after eleven years of childlessness has repeatedly been attributed to medical advice given by Fernel, and there was much speculation in the succeeding years as to what the advice was that appeared to prove so effective. There is no proof, however, that Fernel was consulted in this respect.

During his period of literary productivity in medical science he published much besides the *Medicina*. His *De abditis rerum causis*, which passed through thirty editions, is perhaps best known, but his treatise on venereal disease (*De luis venereae curatione perfectissima*) and his case reports (*Medicinalium consiliorum centuria*) were also very widely read.

THE 'MEDICINA' AND ITS PHYSIOLOGY

Fernel's complete *Medicina* appeared first as a folio of 630 pages, counting title pages, indices and prefaces, published in Paris by André Wechel in 1554, with the usual notation *cum privilegio regis*. It is dedicated in a scholarly introduction to Henry the Second. The official authorization of publication is dated November 18, 1553, and Fernel is designated *Regis Consiliarus et Medicus*, although, as noted above, he did not accept the unqualified position of physician to the king until the death of Louis de Bourges in 1556. Fernel, as in all his writings, latinized his name as Ioannes Fernelius, adding Ambianus, testifying to the region of Amiens as his original home.

The volume is divided into three sections designated respectively Physiology, Pathology, and Therapy. The first part, on "physiology," which had been printed separately in 1542 under the title *De naturali parte medicinae*, consists of seven books, of several chapters each, and with it we may begin our examination of the penetration of pathological anatomy, as well as the understanding of normal anatomy, in the best medical thought of the time. It must be recalled that

Fernel lived in the midst of the most glorious period in the development of anatomical knowledge. He was a contemporary of Vesalius, Columbus, Fallopius and Eustachius. He came two centuries after Mondinus, Henri de Mondeville and Guy de Chauliac. Antonio Benivieni of Florence had written his *De abditis nonnullis ac mirandis morborum et sanationum causis*, Benedetti his *Anathomia*, and numerous other works, and Fracastorius his *Syphilis sive morbus gallicus* and *De contagione et contagiosis morbis et eorum curatione*. Berengario da Carpi at Bologna, and Fernel's fellow Parisians Jacobus Sylvius and Charles Estienne, were writers of his own time.

But no one of all these authors is mentioned in the *Medicina*. The latter was a true product of the Revival of Learning, which brought the Greek and Roman classics back to Europe. The *Medicina* appears to be built almost exclusively on the Greek texts and Fernel's own experience. In the dedication to Henry he lists his sources as Hippocrates, Herophilus, Diocles, Archigenes, Galen, Aretaeus, Aetius, Paul, Alexander, Actuarius and "the Arabians," noting the succession of Greek, Roman and Arabian control of medical philosophy. In the Physiology he refers copiously to Aristotle and occasionally to Avicenna and Averrhoes. Over and again he refers simply to "the Greeks."

The opening book of the section on physiology is entitled *De partium corporis humani descriptione*. In sixteen chapters and sixty-eight pages Fernel reviewed the anatomy of the human body. It is Galenic anatomy, without the admitted addition of the sixteenth century discoveries. At times he appears to disagree mildly with tradition, as in his account of the liver, which is described as consisting of five parts (*fibras*) "called by the Greeks λοβοὺς," although, as he says, as seen by himself, and that not rarely, it was solid, not divided into parts. The distinction, however, he did not seem to regard as important.

Since Fernel is often credited with the first description of appendicitis (not in the *Medicina* but in the posthumous *Universa Medicina* of 1567), one looks for a description of the vermiform appendix, which was clearly shown in the figures by Vesalius, although not named, in the *De humani corporis fabrica*. Fernel's description of the intestinal tract consists of approximately a folio page covering the pylorus (but not the duodenum), the jejunum, the ileum, the caecum, the colon and the rectum. The relation of the caecum to ileum and colon is noted, but there is no mention of the appendix.

After the section on anatomy the *Medicina* treats successively of the *Elements; Temperaments; Spirits and Innate Heat;* the *Faculties of the Mind; Functions and Humors;* and finally the *Procreation of Man*. The humoral physiology of the ancients did not die for many years after Fernel's time, and Fernel's successors looked upon his exposition of the humoral derangements of the body as the most logical, the most orderly and systematic in its arrangement, and the most polished in its literary presentation in that period of medical history.

THE PATHOLOGY OF THE 'MEDICINA'

The section on "pathology," perhaps the first comprehensive text ever so designated, consists of seven books divided into one hundred and twenty chapters. There are two hundred and thirty-eight pages of beautifully printed folio text. The seven books are designated *Diseases and their Causes; Symp-*

toms and Signs; Pulse and Urine; Fevers; Diseases and Symptoms of Parts; Diseases of Parts Below the Diaphragm; and *Abnormalities of the Exterior of the Body.*

It is this section that we should examine most closely for an understanding of the degree of penetration of pathological anatomy in the medical concepts of Fernel's time. The first book is devoted to theoretical considerations on the nature of disease, which is defined quite simply as *affectus contra naturam corpori insidens.* In the light of modern knowledge this opening chapter is an extraordinary combination of the old humoral pathology and an earnest effort to assign an organic seat to clinical entities.

The book on *Symptoms and Signs* is important if for nothing more than its clear distinction between these two sources for accurate diagnosis, a distinction every medical student is supposed to make and one which not a few fail to understand. The third book, on *Pulse and Urine*, is a clinical text dealing with two types of examination long in vogue and intensively cultivated by physicians. It was a day when the quackery of uroscopy was flagrant, but Fernel studied urine in every way that the times permitted, as a "serum secreted from the blood by way of the kidneys," and hence modified by factors related to the blood, as the strength of the pulse, and the condition of the kidneys. Quite naturally the excessive excretion in diabetes was attributed to a fault of the kidneys. In the chapter on matter mixed in the urine it is evident that he was not ahead of his time on the supposed relations of the various sediments to visceral disease.

In the fourth book, on *Fevers*, the latter are meticulously classified, more or less as fevers were classified from the time of Hippocrates, and as they still are to a certain extent, on a chronological basis, as "ephemeral," "continuous," "quotidian," "tertian," "quartan," "intermittent," and "mixed," and descriptively or etiologically as "putrid," "hectic," "malignant," and "pestilential." The search after anatomical localization is apparent in his distinction of pestilential fevers, some of which, he stated, are unaccompanied by indications of their origin, while others exhibit definite organic lesions, with which they can be correlated. In the latter class were the fevers associated with carbuncle and the buboes of plague.

Occasionally a case record is given in the book on fevers. One such is supposed to illustrate the relation of bile and fever. It concerned a middle aged man subject to daily "bilious vomiting." With sudden cessation of the vomiting came pain in the stomach and repeated chills like the chills of fever, but without the latter. Later "the bile putrefied," and thereupon the tertian type of fever ensued, in the course of which the patient died. It is difficult at this late date even to guess at the malady concerned. Unfortunately the necropsy, although it satisfied Fernel, does not enlighten us. "On dissection of the body we found the cause of the many troubles, a pure bile of leek-green color, of a pound's weight, encompassed by membranes in the cavity of the liver, a portion of which had slipped into the nerves of the spine." If there is anything of value here at all, it is the suggestion of a distended gall-bladder. But the account is far too brief; unfortunately it is characteristic of Fernel's necropsy reports. It is often futile to attempt a diagnosis from them. In this case the primary fault was thought to be failure to get the bile out. During the stage of vomiting health was not much impaired. With cessation of the vomit

there was pain and later fever. Both were credited to bile which previously had been evacuated. The finding of abundant bile in the gall-bladder seemed to fit the theory.

Necropsy reports are fairly frequent in the *Medicina*, but commonly the dissection, regardless of the findings, seemed simply to justify the physicians present in an already formed opinion. One cannot avoid the impression that at this stage in the development of morbid anatomy, dissection was often not objective, but simply a new tool used to substantiate deeply ingrained beliefs.

The fifth and sixth books, devoted respectively to the *Symptoms and Diseases of Parts* and *Diseases of Parts below the Diaphragm*, come closest to being treatises on pathological anatomy in the modern sense. Book five begins, like most of the clinical-pathological texts of the succeeding two centuries, with a chapter on pain in the head and its supposed causes, which are none too clear today. Then follow chapters on apoplexy, diseases of the eyes, diseases of the ears, abnormalities of the face and mouth, and finally diseases of the lungs and the thoracic cavity and the heart. In the field of neuropathology, we may note that the explanation of paralysis is by no means, as might be expected, entirely humoral in character. Hemiplegia and paralysis of more complete nature are distinguished. The atrophy commonly succeeding is noted. A noteworthy comment is the following: "The primary seat of the trouble must be sought diligently. If the part deprived of sensation is the face, the trouble is in the nerves coming from the third division of the brain, but if there is loss of movement, the cause is in the first vertebrae of the spine. If all parts below the face are affected, it is the beginning of the whole spine that is involved. . . . When the paralysis takes in one or both legs, the cause is to be sought below the loins. If the spinal cord is affected transversely, the injury involves all parts below, right and left, but if only one part of the cord is injured, only the same side is affected." Fernel emphasized "the necessity of knowledge of every distribution of the nerves". To be sure, he continued with a fanciful explanation of the cause of interruption of the influence of the animal spirit, which he said ordinarily was a crude phlegm tightly attached to the nerve, preventing proper distribution of spirits to the part supplied by the nerve. He added that another kind of humor attached to the spine can cause paralysis, often arising from the yellow bile which is thrown on the spine and the origins of the nerves at the end of intermittent fevers. However, we do not know, today, just what happens when a nervous impulse is transmitted, and hence in the last analysis we cannot say what is not transmitted when the capacity to transmit impulse is lost. But modern authors are not afraid to admit it. One of the chief faults of the medical middle ages was the lack of courage to confess ignorance. The strange mixture of fancy with fact in Fernel's thought is indicated by the continuation of this discussion, in which he related paralysis of a part to a callosity or tubercle of a nerve, to a tumor pressing on the nerve concerned or on the spinal cord itself, or, finally, luxation of the spine.

How much pathological anatomy Fernel actually saw, and how much he imagined or deduced, it is hard to say. The practice of post-mortem examination must have been growing rapidly. There is every reason to believe that exactly the same distinction held then as now between dissection for purposes of an-

atomical understanding and necropsy to learn the cause of death. Sylvius and Günther were supervising dissections before large audiences in the anatomical theaters in Paris. Indeed Vesalius himself participated in these occasions in Paris in Fernel's own time. And Fernel and his colleagues, resting for the moment on accepted normal anatomy, practiced quicker dissection on occasion to learn the anatomical seat of a particular disease. It is rather notable that, whereas Fernel's predecessors, such as Benivieni, limited their pathological anatomy to individual case reports, Fernel generalized on the basis of series of cases, not separately described, of the malady in point.

The last three chapters of the fifth book, dealing with diseases of the lungs, the thoracic cavities and the heart, are of particular interest. In them we see the gropings of the time for anatomical localization. One looks naturally first for the two commonest diseases of the lungs, pneumonia and tuberculosis, and finds both, and both very crudely described. The first of these chapters opens by listing the diseases of the lungs as intemperies, obstruction, peripneumonia, cavity or abscess, and tabes. With the first two we shall not delay. The rest include lobar pneumonia and ulcerative tuberculosis. The descriptions are not good enough to tell what they comprise in addition.

Pneumonia is delineated as an inflammation of the lungs, either phlegmonous or erysipelatous in character, a distinction without much meaning, leading one to wonder if Fernel was reporting observation or theorizing. The rest of the account is clinical.

Cavity (*vomica*) is treated as a disease distinct from phthisis (*tabes*), although the latter is defined as an ulceration of the lung gradually leading to consumption of the body, and it is stated that consumptives are especially prone to cavities. It has taken a long time to bring the multiform manifestations of tuberculosis under one covering concept. Fernel's descriptions of the disease, however, appear to be based on personal observation, for, after citing the case of a young man who had suffered from pulmonary hemorrhage, he wrote, "Not a few are snatched from life in the space of a quarter of an hour, in whose bodies dissection reveals no other cause of death than the sudden rupture of a cavity in the lungs." His explanation of death, in such cases, however, is to us bizarre. The sudden opening of the cavity was believed to "throw pus against the heart, extinguishing its strength and overwhelming it." The fibrosis that must have accompanied the excavations, and the evidence of tuberculous spread to other parts, if the cases truly were tuberculosis, must have been overlooked in the satisfaction at seeing so conspicuous an anomaly as a hole in the lung. A detailed and not inaccurate picture of the clinical course of phthisis, with its variability, follows. Stress is laid on its insidiousness. The disease is attributed to one or the other of two causes, a predisposing hereditary pulmonary constitution and a corrosive humor from the head, an old Hippocratic concept.

In the next to the last chapter, Fernel wrote of the diseases of the thorax. With pleural effusion and empyema physicians had been familiar since ancient times, and Fernel's account is faithful to tradition. A note of special interest is his record of "hard tumors fixed to the root of the diaphragm, gradually consuming the sufferer with tabes", a reference suggesting the swollen lymph nodes of tuberculosis or carcinoma, or

possibly one of the other diseases of the lymphatic system.

After this we come to Fernel's brief account of diseases of the heart. There is little of value here. In stereotyped fashion the diseases are listed as simple intemperies (a word hard to translate), phlegmon, erysipelas, tumors, ulcers and wounds. Obviously this is systematization from theory for the most part, not from factual observation. The text under the heading is devoted to symptoms of vascular disturbance. Understanding of the pathology of the heart, in the middle of the sixteenth century, was undeveloped. Fernel did call attention to clots found in the heart, stating that in "two who died suddenly after vigorous exercise at ball, we found the bile coagulated into a sort of black tophus." Presumably he and his associates at the autopsy were observing the post-mortem clots that engaged the earnest attention of anatomists for nearly three centuries, beginning a half century before the publication of the *Medicina.* There is brief reference to arterial aneurysm, presumably aortic aneurysm, without citation of specific cases, a lesion which in the next few years was to be described repeatedly.

Book six is notable for its references to truly existing anomalies of the alimentary tract, the liver and the kidneys. In the opening chapter what is presumably a carcinoma of the esophagus is described, "a hard tubercle obstructing the entrance to the stomach." Carcinoma of the stomach is also apparently pictured, although the expression is less clear, and there is no citation of specific cases. The delineation of ulcer is recognizable, and the reference to its occurrence following the ingestion of caustics seems to indicate that Fernel had definite cases in mind.

Diseases of the liver are listed as intemperies, obstruction, scirrhus, inflammation, abscess and ulcer. This is the usual stereotyped systematizing to which Fernel was prone. Under the heading Obstruction, as might be expected, there is reference to calculi in the gall-bladder. However, the term is used primarily with reference to vascular obstruction. The relation of portal vein and vena cava to the circulation of the liver was understood. Indeed there is a suggestion of the capillary circulation in the account: "Obstruction of the liver is common; no viscus is more subject to this fault, because the portal vein, divided into the finest branches, loses itself in the substance of the liver; other branches, not less thin, come together in the vena cava, so that all nourishment is carried through and borne out." The character of the obstruction that might ensue is pictured very vaguely. A crude humor is primarily implicated. A phenomenon apparently correlated was over-long retention of yellow bile in the liver, without its normal evacuation, with resulting petrifaction in the gall-bladder. Biliary calculi were well known. Most of the early anatomists described them. Fernel recognized obstructive jaundice, referring it to "blocking of the duct whereby the bile is carried from the liver or of the duct through which it is evacuated into the intestine." A distinction is drawn between pigmented calculi and calculi floating in water (i.e., cholesterol). One case is cited in which a single large calculus filled the gall-bladder.

"Scirrhus" of the liver is described as an abnormal hard tumor, developing without pain. The term covers much, and the account is highly vague. Simple increase in size is included, and the possibility of diagnosis of an enlarged liver by palpation is noted. The exposition is so poor, however, that secondary tumor,

which must have been common then, as now, cannot be identified. However, a relation to ascites is noted. The explanation is entirely humoral and theoretic. Under the heading inflammation of the liver are references to abscess and ulceration that may mean tumors, but the account is too obscure to understand. Cirrhosis cannot be recognized in the chapter.

It is not surprising that no definite pathological entity can be identified in the chapter on diseases of the spleen. This organ fascinated the ancients, and around it they built a pathology quite foreign to modern thought. A relationship with the liver was recognized, because of the close vascular connection. The spleen was looked upon as the peculiar receptacle of the black bile, just as the yellow bile belonged to the liver. Fernel devoted a special chapter to the *Symptoms of the Liver and the Spleen*, indicating a belief in their interdependence. It is chiefly devoted to the subject of icterus, and is rather remote from the field of pathological anatomy.

The account of intestinal anomalies is largely concerned with obstruction of the bowel, and the text deals with both its symptoms and the anatomical states concerned. Extreme constipation is described, which "comes sometimes, although rarely, from a tumor (*tumor praeter naturam*) arising in the substance of the intestine, which may grow to such a degree that it fills the lumen and closes the passage." A case of complete obstruction of the colon by a tumor mass is described. Reference is made, as in the case of almost all organs, to abscess and ulcer. Nothing definite can be recognized under these headings, although there is a note that ulceration may "end in cancer". Altogether there is good reason to believe that Fernel was familiar with carcinoma of the large bowel. Dysentery is referred to ulceration of the intestines, but apparently on the basis of the bloody dejections rather than the appearance on dissection. Rather lengthy reference is made to distention of the intestine by gas, which Fernel stated he had observed in the dissection of "not a few persons, in whom the dilatation reached the size of an arm."

In conformity with his usual custom, diseases of the kidneys are listed in order as inflammation, obstruction, abscess and ulcer. "Inflammation of the kidneys, or nephritis," was considered rare, "because their firm and hard flesh admitted a fluxion only with difficulty." On the subject of obstruction, however, Fernel could write at length. Gravel and stone were well known. Indeed, the description of renal calculi is one of the best accounts in the whole book. Such sentences as the following indicate clearly that the descriptions were based on frequent observation at post-mortem examination: "So we often observe the entire flesh or substance of the kidney eaten away, and the pus and many calculi wrapped up in a membrane, much like a pouch," and "In those who have already long been used to nephritic pains I have at times found the ureter dilated to such an extent that the large finger could be inserted into it." The clinical course is well delineated.

The succeeding chapters of book six deal with diseases of the genital system. In the description of the uterus are accounts in which without much hesitation one can recognize cancer of the cervix and myomata. Carcinoma of the cervix had been known for centuries. The teaching, repeated by Fernel, of "a malignant ulcer of the uterus, degenerating into carcinoma" must have been the accepted one. The observation of ul-

ceration into the bladder and the intestine, with resultant evacuation of urine and feces through the vagina, corresponds with well-known clinical facts.

Thenceforward book six and book seven deal largely with principles well known from obstetrics, surgery and clinical examination of accessible parts, rather than with diseases to be studied intimately only by dissection, and here, therefore, we may leave the subject of pathological anatomy as it is portrayed in the *Medicina* of Jean Fernel.

To complete the record, however, we should pay brief attention to the third section of the *Medicina*, the last of the three major divisions. This is devoted to "therapy", and is concerned entirely with the two outstanding methods of treatment, blood-letting and purging. The references outside of his own experience are to Plato, Hippocrates, Dionisius and Avicenna. Strangely, the polypharmacy of the time is omitted. It may be added, however, that in a subsequent edition brought out by Plancy (1567) four books were added to the original three in this section, and in these the drug treatment of disease is presented in abundant detail.

THE NECROPSY OF JEAN FERNEL

It is perhaps appropriate to close this paper with an account of Fernel's own last illness and post-mortem examination. It is found in the biography by his student Guillaume Plancy (*Vita Ioan. Fernelii*, in the *Opera* of Fernel, Frankfurt, 1607) and is cited in somewhat condensed form in the *Sepulchretum* of Théophile Bonet. It begins with an account of the last sickness of the wife of Fernel. She fell ill with fever at Fontainebleau and passed away two weeks later. Fernel was prostrated by her death, and, as the story relates, from extreme grief and distress of mind himself fell into a continuing fever. On the seventh day of his illness he seemed to be improving. The urine was becoming clear and the fever was lessening. A favorable outcome was anticipated by his physicians. On the eleventh day, however, the patient took a turn for the worse. The urine again appeared to be abnormal, and distressing symptoms reappeared. Other physicians were brought in. It was recalled that some time previously Fernel had suffered from a quartan fever, from which he had never fully recovered. His addiction to fluids, particularly cold water, was cited as predisposing to illness, for this was believed to have a bad effect on the spleen. His present trouble was considered an acute exacerbation of previous difficulties. For two years he had been afflicted with sourness in the mouth and throat, which he had not been able to dispel by any remedy. The death of his wife was regarded as the final blow. A humor was thought to have collected in the spleen, and gradually to have grown hot and finally putrefied. The inflammation of this organ was believed to be the cause of the continuous fever which exhausted his strength. Death occurred on the eighteenth day of his illness.

"Investigating the cause of his death by dissection", says Plancy, "we judged it to have resulted from inflammation of the spleen, for this organ was swollen, livid and turning green; when opened by the scalpel it let out a great quantity of bloody fluid resembling the blackest pitch."

So died one of the brightest lights of French sixteenth-century medicine. What the real cause of his death was we can never know. The account of his last illness and the necropsy illustrate as clearly as his own book the vagaries of the medical practice of his time, but

equally well they point to the growing effort to identify the symptoms of illness, however general, with a fault of some particular organ. Few besides Fernel in the first half of the sixteenth century taught clinical medicine in the light of pathological anatomy. In the second half of the century observations from the necropsy table accumulated rapidly. The custom of the pathological case report developed. But the "*saepe vidimus*" of Fernel, frequent in the *Medicina*, indicates that even in the first half necropsy had become common. The course had been laid thus early for objective study of disease.

Memoir of John Norman Henry, M.D.*

By Francis W. Sinkler, M.D.

JOHN NORMAN HENRY, a Fellow of the College, died October 4th, 1938. He was born in Philadelphia, September 12th, 1873. His father was Dr. Frederick P. Henry, who is remembered affectionately by the older Fellows as the Honorary Librarian of the College for 29 years. The elder Henry introduced a resolution to the College, which authorized the solicitation from the Fellows and from the public of money for an Endowment Fund for the Library. This resulted in the collection of more than fifty thousand dollars, for which the College owes Dr. Henry a lasting debt of gratitude.

Norman Henry was educated at the Episcopal Academy and St. Paul's School, received the degree of A.B. from the University of Pennsylvania in 1893, and that of M.D. from the same institution in 1895. He served as Resident Physician at the Children's Hospital, and later at the Pennsylvania Hospital.

The following professional appointments were held by him at various times: Physician to the Pennsylvania Hospital, Clinical Professor of Medicine at the Woman's Medical College of Pennsylvania, and Assistant Physician to the Philadelphia General Hospital.

Through his terms of office as President of the Philadelphia County Medical Society, and as President of the Medical Society of the State of Pennsylvania, he contributed largely to the cause of the medical profession.

Dr. Henry's non-professional activities included the following: President of the University Club of Philadelphia; President of the General Alumni Society of the University of Pennsylvania; President of the Associated Clubs of the University of Pennsylvania; Trustee of the University of Pennsylvania. Also he was a founder and director of the Big Brother Association, and Manager of Christ Church Hospital.

Dr. Henry was a member of the Medical Reserve Corps with the rank of First Lieutenant, and on December 19th, 1917, he was commissioned as Major in the Medical Department of the United States Army. He served for six months in the United States, and for seven months in France, being Chief of the Medical Division of Base Hospital #38. He acted as Commanding Officer of the Base Hospital from October 1st to November 15th, 1918, during the incapacity of the Commander. He was discharged with the rank of Major on February 16th, 1919.

He was elected to the College in March 1903, and was a member of the Hall Committee from 1911 to 1923, thus giving twelve years of useful effort to this institution.

An important and valuable contribution to the College consists of his history of the College in the Founders' Week Memorial Volume, published in 1909. This history is based on Ruschenberger's history of the College published in 1887, but Dr. Henry's history narrates the important events from 1887 to 1909, and it includes a list of the officers from the foundation to 1909.

*Read at the Business Meeting of the College, January 6, 1941.

The outstanding accomplishment of Dr. Henry was his administration of the Department of Public Health of Philadelphia from 1932 to 1935, inclusive. His term of office occurred during the most severe depression years, and as a consequence there was a great increase in demand for the services of the City institutions. During the same period the administration of the City was conducted with rigid economy by the Mayor and the Council; so that the budgets for all departments were reduced to the minimum. In spite of this handicap, the success of his administration can be measured by the general mortality record of the City of Philadelphia during his term of office from 1932 to 1935, when the average rate was 12.11 per 1000, this being the lowest death rate established for Philadelphia up to that time. This may be compared with the record from 1928 to 1931 of 13.10 per 1000.

Among the notable events during his incumbency were the re-establishment at the Philadelphia General Hospital of the Saturday morning clinics, which had been discontinued in 1917; and the dedication of wards at the Philadelphia General Hospital as memorials to those who there had done conspicuous work. Also research was started in the old Tuberculosis Pavilion during Dr. Henry's administration, with funds provided by an outside organization. The Osler Memorial, dedicated during the past year, was instituted during Dr. Henry's term of office.

The most important performance of Dr. Henry's administration, and one which is considered to be a memorial to him by his many friends in the Department, was the establishment in Philadelphia of active immunization against scarlet fever in charitable institutions and the public schools of Philadelphia. To effect this, Dr. Henry journeyed to Chicago and persuaded Dr. Gladys Dick to coöperate. With great difficulty he obtained an appropriation from Council to provide for this work. He debated the subject before the County Medical Society and with other groups of physicians, some of whom were opposed to the procedure. He addressed the Managers of charitable institutions, and the parents of the children to be immunized. Owing to Dr. Henry's efforts, assisted by the successful results obtained by his Department, immunization, which was started in 1932, had become an accepted procedure in 1935. In his report for the last year of his service Dr. Henry stated that not one case of scarlet fever had been reported in any individual who had been given the Dick Test.

Dr. Henry was possessed of a fine physique and was a natural athlete. He was a member of an International Cricket Team, and he continued to enjoy all forms of exercise and sport up to the end of his life. He was a man of great personal attraction and made friends easily. He was enthusiastic in his approach to problems, and had an unusual vitality and zest for life, which stimulated and gave pleasure to all of his associates. He was deeply religious and served for many years as a Vestryman of St. Peter's Church in Philadelphia.

Memoir of Alfred Stengel, M.D.*

By William Pepper, M.D.

ALFRED STENGEL, the 29th President of this College, was born in Pittsburgh, Pa., on Nov. 3rd, 1868. His father, Gottfried Stengel, a civil engineer, had come to this country about 1850 from Germany, one of those who, disapproving of conditions in their home country, came to the United States at that time and added materially to our own civilization. He was one of six sons; an older brother, Walter, was likewise a physician.

Alfred Stengel came to Philadelphia from Pittsburgh to study medicine at the University of Pennsylvania in 1886; he was then almost 18 years of age. The course was then but three years in length. No college pre-medical work was required and he had had no college training. Nevertheless, he graduated third in his class with a general average of 96.9, only two-tenths of a point behind Thomas J. Harris, who was first with 97.1. About one-fourth of his class, that of 1889, had graduated from College. For a young man with such preparation to become later a prominent figure in the medical profession, a Professor of Medicine and a frequent contributor to medical literature, demanded intelligence, ambition, self-education and hard work. That men with such meagre preparation for the practice of medicine should succeed as Alfred Stengel did, might by some be considered as proving that our present requirement of four years of college pre-medical work and four years, instead of three, of work in the Medical School is unnecessary; but it must be borne in mind that there is much more to be learned today than was the case fifty years ago.

In his last year in the Medical School Alfred Stengel was one of those students selected to be included in Eakins celebrated painting of the Agnew Clinic. He is pictured as a youthful, smooth-shaven lad, in those days of bearded medical students. His head rests on the shoulder of a fellow student, Clarence A. Butler, whose head rests on the top of Stengel's. They do not appear to be sleeping, but merely endeavoring to see without much success the finish of the operation just performed by Dr. Agnew.

No one examining the faces of the students portrayed in the painting would select Alfred Stengel as the one most likely to make a name for himself in medicine.

Less than half of the Class of 1889 served an internship, but Alfred Stengel won a place at the Philadelphia General Hospital, where he spent fifteen months. Then, at the age of twenty-two, he was ready to practice his profession. He tells us in a memoir he read on Dr. Allen J. Smith that Dr. Smith helped him to obtain a subordinate position in the Pathological Department at the University, but as in those unhappy days such appointments carried with them little, if any, emolument, it was necessary for him to seek some outside sources of revenue, in practice, quizzing or writing. Dr. Smith himself, laboring under the same necessity, had however an office and invited Dr. Stengel to live with him and share it. But this friendly arrangement came to an end when Dr. Smith left to accept the Chair of Pathology at the University of Texas in the fall of

* Read at the Business Meeting of the College, January 6, 1941.

1891. However, before he left he nominated Dr. Stengel as his successor in the Medical Institute, as quizz master in pathology, and turned over to him all his notes and preparation for this work. The experience gained in conducting these extra-mural quizzes was excellent training for those who later were appointed to teaching positions. In 1893 he was elected Pathologist to the German Hospital. In 1892 he gave up his Quizz Class in pathology and began quizzing in medicine.

In the Spring of 1892 he became the office assistant of Dr. William Pepper, then Professor of Medicine and Provost of the University. This position he held for three years, and then, with the opening of the William Pepper Laboratory of Clinical Medicine, he became Assistant Director of the Laboratory. A few years later Dr. Pepper made him Director and he served as such until 1911. In 1893 he was made Instructor in Clinical Medicine in the University's School of Medicine and thus began his official connection with the University which lasted until his death. In 1897 he was promoted to Professor of Clinical Medicine and in 1911 to Professor of Medicine. In 1937 he was elected Emeritus Professor of Medicine. From 1896 to 1898 Dr. Stengel also taught at the Woman's Medical College as Clinical Professor of Medicine. He was a great teacher, clear, concise and with a keen appreciation of the importance of stressing in his lectures, clinics and seminars the really important facts which should be learned by his students. In 1895, being then twenty-seven years of age, he was elected Physician to the Philadelphia General Hospital. Later he also served on the medical staffs of the Howard, Children's, Pennsylvania and University Hospitals. In 1898 he accepted the editorship of the *American Journal of the Medical Sciences*.

In 1902, 1903, 1904, as editor of the American edition of Nothnagel's "Encyclopedia of practical medicine," he labored hard before this twelve volume work was successfully brought to press.

In July 1898 my father died, and then began the close association between Dr. Stengel and myself that lasted for forty-one years. I had just finished my internship and it seemed wise that some effort should be made to carry on my father's large office practice. Therefore, I proposed to Dr. Stengel that we become partners and share my father's office together. He agreed, and so until 1912 he had his office at 1811 Spruce Street and for about ten years he lived with us practically as a member of our family.

He also spent for some years his summer vacation with us in my mother's house at Northeast Harbor, Maine, and there he had his own boat which he sailed in the races. He played tennis, swam and climbed mountains.

In 1909 Dr. Stengel married Martha Otis Pepper, daughter of William Platt and Alice Lyman Pepper. As William Platt Pepper was my father's first cousin, Alfred and I were even more closely bound together than before. Three children were born, two boys and a girl. His older son graduated in medicine in 1935; the younger studied law. Dr. Stengel bought 1728 Spruce Street and had his consulting office there from 1912 until, with the completion of the Maloney Clinic at the University Hospital in 1939, he moved his office to the Hospital. In 1914 he bought a farm near Newtown Square and built an attractive summer residence there. He farmed his land and in his spare moments played the part of the proverbial gentleman farmer.

Dr. Stengel was a prolific writer and his bibliography is an extensive one. His earlier articles are chiefly on hematological or pathological topics; later his

interest in clinical medicine is apparent. He wrote the section on Diseases of the Blood in the "Twentieth Century Practice," on Diseases of the Intestines in Osler's "Modern Medicine," and (with Dr. Richard A. Kern) on Diseases of the Liver and Gallbladder in "Nelson Loose-Leaf Medicine." His one book was his very successful "Text Book of Pathology," the first edition of which was published in 1898. Eight editions have since appeared; and in the fifth edition Dr. Herbert Fox collaborated as joint author.

It is appropriate to recall also the splendid service Dr. Stengel rendered the University of Pennsylvania as an administrator. In 1928 he was elected a Term Trustee to serve for ten years and in 1931, with the change in the administrative system at the University, he was made Vice-President in Charge of Medical Affairs. In this position he had under his care the School of Medicine, the Graduate School of Medicine, the Dental and Veterinary Schools and all other medical affairs of the University. He was a Manager of the University, Graduate, Orthopaedic, and Veterinary Hospitals, a Manager of the Wistar Institute and later President of its Board. He was a member of the University Committee of the Henry Phipps Institute. To these, and many other University duties, he gave his time and unselfish service.

The need at the University Hospital for a building or wing to house various clinics, laboratories, outpatient departments, etc., was early recognized by him. The Martin Maloney Memorial Clinic stands today as a monument to Dr. Stengel's foresight and planning. He persuaded Mr. Maloney to contribute the money needed for its erection. It stands on the site of the old Pepper Laboratory building on the corner of 36th and Spruce. It was opened in 1929. One floor of the ten-story building now houses the Pepper Laboratory. In the impressive lobby of the Maloney Clinic hangs the excellent portrait of Dr. Stengel by Mr. Johansen. All other portraits of former Professors of the medical faculty hang in the Medical School, but his portrait has been appropriately placed in the Maloney Clinic for which he did so much.

Dr. Stengel was a member of the American Philosophical Society, the Association of American Physicians, The American Pediatric Society, the American College of Physicians, of which he was President, and he was a Fellow of the College of Physicians of Philadelphia, which he served as President from 1934 to 1937.

He was the recipient of honorary degrees from the Universities of Pittsburgh, Lafayette and Pennsylvania. He was a Major in the Medical Reserve Corps of the U. S. Army.

Busily engaged, chiefly with his administrative duties, and in apparently perfect health, Dr. Stengel died suddenly on April 10th, 1939, he then being seventy and one-half years of age. The University of Pennsylvania lost a very valuable servant, Philadelphia a civic minded citizen, and a host of former students, patients, colleagues and acquaintances a well beloved and admired friend.

I find myself comparing on the one hand the Alfred Stengel pictured in the Agnew Clinic, the youthful, penurious, untrained boy who came to Philadelphia unknown, without friends or relations and who by his own effort, brains and native intelligence rose to a commanding position in medicine in this country; and on the other hand, the man shown in the portrait in the Maloney Clinic who finally had had accorded to him his well won honors.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

Meeting, December 20, 1940

(Dinner meeting. Speaker: Joseph Stokes, Jr., M.D.)

SECTION ON OPHTHALMOLOGY[1]

Meeting, December 19, 1940[2]

Adie's Syndrome: Presentation of a Case. Thomas H. Cowan, M.D.

Multiple Sclerosis as an Ophthalmoneurological Condition. Walter I. Lillie, M.D.

Surgical Treatment of Retinitis Pigmentosa. Francis C. Grant, M.D.

Diagnostic Significance of Lid Retraction. Francis H. Adler, M.D., and Harold G. Scheie[3], M.D.

Third Cranial Nerve in Intracranial Pathology. Joseph C. Yaskin, M.D.

Moving Picture Projection of Neuro-ophthalmological Conditions. A. M. Ornsteen, M.D.

[1] The transactions of this section are abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology*.

[2] Joint meeting with the Philadelphia Neurological Society.

[3] By invitation of the Section on Ophthalmology.

SECTION ON OTOLARYNGOLOGY[4]

Regular Meeting, December 18, 1940

Relation of Voice to Hearing

Relation of Hearing to Distance from the Source of Sound. Robert J. Hunter, M.D.

Functional Changes of the Larynx in Relation to Voice Production. Robert F. Ridpath, M.D.

Pathological Changes in the Larynx in Relation to Voice Production. Louis H. Clerf, M.D.

Voice Characteristics in Deafened Children. Walter Hughson, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

Meeting, December 2, 1940

Chronic Carbon Monoxide Intoxication as a Domestic and Industrial Hazard. Heinrich Brieger*, M.D.

Physical and Chemical Factors in the Causation of Silicosis. Theodore F. Hatch*, M.S.

[4] The transactions of this section are abstracted in the *Archives of Otolaryngology*.

* *By invitation.*

President's Address*

Edward B. Krumbhaar, M.D.

IT IS a pleasure, in complying with the College ordinances and by-laws, to be able to report another successful year in our College history. I also take the opportunity to express my appreciation of the great honor of having been elected your president. The occasional selection of a follower of the preclinical sciences seems to me a desirable recognition of the close affiliation that these sciences have with clinical medicine and with the objects for which this College was founded. Our list of 30 Presidents shows that the clinical specialties have also been but scantily represented thus far. One would not expect to find specialists in our first century, to be sure; but of the 19 presidents of the past 53 years only 4 come in this category, a neurologist, an ophthalmologist, an oto-laryngologist, and a genito-urinary specialist. Doubtless hereafter this list will be increased as the occasion arises.

The *scientific meetings* of the College and its sections, certainly one of our two most important contributions to medicine, have been held regularly, and the standard of presentations well maintained. If one may judge by the average attendance, which at the College meetings is now regularly several times as great as it was 10 or 15 years ago, the method of filling the College programs with the endowed lectureships is working well. In the past year, we had an Anders lecture given by Dr. Charles Armstrong of the United States Public Health Service on the viruses of choriomeningitis and poliomyelitis; two Hatfield lectures, by Dr. Robert B. Osgood on the medical and social approaches to the problem of chronic rheumatism, and by Dr. George W. Corner on the physiological basis of corpus luteum therapy. Three Newbold lectures were given: Dr. Tom D. Spies spoke on avitaminosis B; Dr. Alvin F. Coburn on rheumatic fever; and F. J. W. Roughton, F.R.S., on blood storage and shock, at the special war preparedness meeting. The annual Mütter lecture was devoted by Dr. Allen Whipple to the work of his Spleen Clinic at Columbia. The triennial Weir Mitchell oration was to have been given at the November meeting by Dr. John F. Fulton; but having been sent unexpectedly abroad by the Government, he found it impossible to get back in time to keep his engagement. The oration, however, is being published in our *Transactions & Studies* (December, 1940), with the added value accruing from his European experience. At the April meeting two of our Fellows spoke by request on aspects of the cancer problem: Dr. Lucké, on tumors in cold-blooded animals and their experimental study, and Dr. McFarland on the pathological diagnosis of cancer in man. Three lectures were given for the general public: by Dr. J. Parsons Schaeffer on the human constitution; by Dr. W. Edward Chamberlain on the X-ray as an aid to diagnosis; and by Dr. Chevalier Jackson on the bronchoscope. At one of these the audience numbered 450, overflowing from Mitchell Hall into the adjoining room. We may accept, I

*Read, January 6, 1941.

believe, that these lectures give the public useful and authoritative information on medical subjects and are slowly but surely accomplishing their other purpose of making our College better known to the citizens of Philadelphia.

The College *Sections* have met regularly through the academic year, on the whole successfully. With the general College meetings now devoted almost entirely to guest lectureships, the meetings of the Sections and those of the other societies that are held in the College building acquire added importance as outlets for our local talent. According to the Clerks of the 5 Sections, the number of paid-up members, the number of meetings, and the average attendance on the whole compare favorably with those of other years. Occasional unfavorable, and sometimes entirely inexplicable, responses to the sectional officers' efforts have occurred and are only to be expected. They may, however, be useful as stimuli to new and better efforts: small attendance not to be explained by the weather, conflict with other meetings or other detectible causes should raise doubt in the minds of the program makers as to current interest in the subjects offered. There are other societies that have regularly met so long in our College building and with audiences composed so largely from our Fellowship that they would differ in but few essentials if they had happened to be College Sections. I hope that we shall always look on them as close relatives and that they will always be as anxious to meet here as we are to have them.

Our splendid *Library* is often and correctly spoken of as the other important contribution of our College to medical Philadelphia. Under the alert management of our Library Committee and our gifted Librarian, Mr. McDaniel, the Library continues to prosper in spite of the difficulties produced by the war. It is really surprising how little interruption there has been to literary work thus far, in view of the number of books and periodicals that have been held up or delayed by war conditions. Needless to say, the library staff is constantly on the alert to keep this inconvenience at a minimum. Though some 2500 fewer issues of periodicals than last year have been received on account of the political situation, all our other "accessions" show a normal increase. The most important forward step of the year was the opening of the Library from 2 to 5:30 (except during the summer months) on Sunday afternoons. As might be expected, the average number of visitors per hour reached its peak on those afternoons, and chiefly, though not entirely, on this account, the number of visitors for the year, both Fellows and Non-fellows, was higher than in the previous year. The holders of special College privileges continue to make good use of our library resources. In fact, the only proposed change in our Ordinances and By-Laws in the past year is designed to expand this group by establishing a fifth category, for representatives of the great commercial houses that are coming constantly in closer touch with scientific medicine. The annual detailed report on the state of the library will appear below this address in the February number of the *Transactions & Studies*.

A great library properly contains much more than just books and pamphlets, and its efficiency depends on the availability of *all* its contents. Our special card index of portraits, even of the humblest journal half-tones, is an example of what I have in mind. The frequent exhibits prepared by our library staff in connection with our own meetings

and those of sister societies constitute another of the Library's educational contributions. Still another came into being this year with the creation of a *Collection of Medical Art* with Dr. Samuel Sturgis as its Director. Dr. Sturgis, who has long been interested in this subject, has not only donated his own valuable and beautifully prepared collection, but is giving much time and energy to arranging our own possessions. Though much remains to be done by the Director in this arduous labor of love, we can already be legitimately proud of a fine collection, well arranged and classified, uniformly mounted, indexed, and cross-indexed, so that its contents are pleasantly and readily available to any one wishing to use it.

Financially, the College continues in a sound condition, if not as affluent as we should like to see it or as current repute unfortunately so often attributes to it. I say unfortunately, as such a reputation not only puts us in a false position but naturally obstructs efforts to get further needed help. Though we have balanced our budget for the past few years, it has been only by the exercise of the greatest care, and occasionally by relinquishing desirable improvements. The cost of living in this country, institutional as well as individual, will very probably be increased in the near future. Unless more unrestricted income can be found to meet the needs of the College, the possibility of additions to our service to the medical community seems small, and even curtailments not improbable. The estimate by the Pennsylvania Company of our capital holdings is but little changed ($2,500 less) from that of a year ago. However, our anticipated operating income, exclusive of the special funds, is $32,457.50, almost a thousand dollars less than that of last year. Fortunately we have had no defaults in income from our securities during the past year. "Turnover" of securities for the usual reasons has been about what was to be expected. Following the recommendation of our financial advisers, we have reinvested mostly in common stocks and in this way our security yield has not been reduced. The unavoidable risks associated with such a policy are recognized, however, and even with today's unprecedented low return from high grade bonds, we must not pursue this policy too far. All these increased uncertainties of income and outgo have indicated that a larger unappropriated balance ($1,237.50) should be withheld in the proposed 1941 budget than has been the custom in recent years. This has been possible, without reducing the various budgets, through the termination of the annuity to Mr. Fisher, of whom I shall speak later. Details of our financial position appear in the Treasurer's report, to be published in the *Transactions & Studies*. Our long deferred hope to sell the property at 13th & Locust Streets was stimulated last spring by a definite "nibble" from a responsible source. Though there was no disagreement as to terms, no formal offer materialized. We are grateful for two welcome financial gifts: the Library benefits by the creation of the Fund of the Friends of George E. Pfahler for the purchase of books on roentgenology and radiology; and the bequest of Dr. John H. Musser, Sr., establishing the Benjamin Musser Lecture in Clinical Medicine, now becomes available. One new portrait adorns our walls—that of Dr. William Zentmayer, presented by the Section on Ophthalmology.

In its earlier days, the College was frequently concerned with the public health of the city and state when its

advice was sought by the authorities. Through its *Committee on Public Health, Preventive Medicine and Public Relations*, this important relationship has been strengthened in recent years. Our committee continues the admirable custom of the past few years of meeting jointly with the committee of the County Medical Society, at present under the chairmanship of our committee chairman, Dr. Joseph Stokes, Jr. During the past year we have had the advantage of having a member of the City Board of Health on our committee and the Director of Public Health closely connected with College activities. Toward state health improvement, the committees' continued study of conditions at Byberry and their support of its superintendent, Dr. Herbert Woolley, have been important factors leading toward the needed improvements—achieved and in prospect—in that institution. In city health matters, several important problems have been studied, and recommendations brought to the sympathetic attention of the city's Director of Public Health. On advice of this committee the pasteurization of all milk entering the city has been recommended jointly by this College and the County Medical Society. Such matters as the regulation of the amount of vitamin D in "Vitamin D milk," the water supply and sewage-disposal program for the city, health examination of food handlers and household employees, district health centres and their proper administration, constitute the problems that this committee has been studying, in one case with the assistance of two sanitary engineers, and in frequent consultation with the Department of Public Health.

From the *Hall Committee* we learn that the College property is on the whole in good condition, though of course repairs and improvements will be needed during the coming year to continue the upward trend in its physical condition. In the words of the Superintendent's report, "the College has benefited enormously through its adoption as a 'worthy project' by the Department of Public Assistance." The fact that this help was obtained by the chairman of the Hall Committee should not be overlooked. These few figures are eloquent: 1,848 hours of skilled labor and 7,312 hours of unskilled, a total of 9,160 hours since March, averaging 33 hours a day, were donated. One can easily see that without this help many of the improvements accomplished in the past year would have been impossible. I am glad to report also that the Superintendent now has the authority to grant the use of Mitchell Hall to any society customarily using the College for its meetings. It is also opened freely to other established societies; to the A. A. A. S., for instance, for its meeting during the Christmas holidays.

The *Transactions & Studies* of the College continues to appear four times a year under the editorship of W. B. McDaniel, 2nd, but, beginning with the April number, in a slightly different and improved format. This not only presents a more readable pamphlet in its double columns, but permits more reading material to appear at a lower cost than formerly. The more important scientific and historical communications form the bulk of the text. One would like to see them better illustrated, if more funds could be made available. It is good to see that most of the endowed lectureships are now printed and thus can be read in full by the whole Fellowship, and with but little delay—I hope that hereafter they can be made available to

the editor for publication without exception. Another wish—shared I know by many others—is that the attractive and informal Fugitive Leaves that appeared for several years in multigraph form might again be found now and then in the *Transactions & Studies*. The programs of the Sections, with abstracts of papers read at the Section on General Medicine, appear in each number; the President's address and annual committee reports now appear promptly in the February number; the personnel of the various committees and the list of College Fellows are published in the April number, again with less delay than in the earlier series. I am sure that in its present form our publication is more useful and more attractive to our Fellows and to the medical world in general than in earlier days, without loss of record value.

In connection with the Bicentennial Celebration of the University of Pennsylvania, the College held a reception in Mitchell Hall on the evening of September 17th for the University's medical guests and their hosts. Several hundred people attended, including not a few Philadelphians on their maiden visit to the College, who thus had opportunity to see at least something of our splendid building and its contents. Weir Mitchell's wisdom in endowing an entertainment fund was once more confirmed.

The Women's Committee on the Sinkler Memorial Garden (the "Friends of the Garden" as they have been called), under Mrs. John H. Gibbon's chairmanship, continues efficiently to maintain the beauty and educational value of this part of the College property. An attractive addition, donated by Mrs. Alfred Stengel, is an ornamental sundial erected in the centre of the herb garden in memory of Dr. Stengel. Toward meeting the heavy expense that they incurred in renovating the garden two years ago the Committee carried through two successful functions. In the spring a plant sale was held in the College building and in the fall Mrs. Caspar Hacker exhibited in Thomson Hall some interesting moving pictures that she had taken on her travels abroad. In spite of inauspicious weather both were financially successful. We are indeed grateful to these ladies; appreciation of their effort is shown in the not infrequent remarks of praise that come to us from College users as well as garden lovers.

On July 14th, the day nominated in the bequest, the *Alvarenga Prize* was awarded to Dr. Ernest Goodpasture, of Nashville, for his distinguished contribution to the knowledge of viruses. The award was combined with an invitation to deliver one of the College lectures in the ensuing academic year. This was accepted and a lecture will be given by Dr. Goodpasture on "The Cell-Parasite Relationship in Bacterial and Virus Diseases" on March 5th, 1941. Thus for a second time in recent years, an improvement has been made in the procedure attending this award. We may now hope that it will not only always reward truly distinguished work, but also that our Fellows will have the opportunity to hear this work described and to read about it in the *Transactions & Studies*.

Medical preparedness in the present national emergency is a problem that has materially concerned the Fellowship and has already begun to affect our activities. A special preparedness meeting was held jointly with the Section on Public Health on November 8th, at which time Francis J. W. Roughton, lecturer on physiology at the University of Cambridge, gave a Newbold lecture on "Blood Storage and Shock," and Lt. Col. A. P. Hitchens,

professor of public health and preventive medicine at the University of Pennsylvania, made recommendations for "A Health Program for the Homeside in Wartime." The latter paper, together with Dr. J. F. Fulton's Weir Mitchell oration, "Neurology and War," may be read in the December, 1940, number of the *Transactions & Studies*. Our library has available a list of important books and articles on military medicine. Several of our Fellows are on the preparedness committees organized by the National Research Council and meet frequently in Washington; many more are enrolled in or organizing medical units to be available for one of the military services. Some are already in the active service of their country.

Our Fellows have taken, as usual, a worthy part in the medical affairs of the country; it so happens that this year they have held the presidencies of the American College of Physicians, the American College of Surgeons, and the American Otological Society; five are sectional officers of the American Medical Association, and a number of others are officers of other national societies or organizations, such as the specialties examining boards. Lt. Col. Hitchens was the official representative of the College at the Eighth American Scientific Congress at Washington last May; Dr. Francis R. Packard at the Bicentennial Celebration of the University of Pennsylvania; and Dr. C. L. Brown at the Pharmacopoeial Convention, at which he was made a member of the important Committee on Revision.

The total College Fellowship now numbers 688, two more than last year. In 1940, 17 were elected to active Fellowship, but we lost by death 12 active Fellows, one non-resident and 2 honorary Fellows. I feel that while we must continue to be most vigilant in the maintenance of the high quality of our membership, we must be equally careful not to let those properly qualified be overlooked through negligence or because it may seem like nobody's special business. We must realize that this entails a gradual increase in the size of our membership, parallel with the growth of the lay and medical population of our metropolitan area. I suspect that a comparative study would show that a considerable correlation has existed between these figures since our foundation.

As usual, it is the President's duty to speak of those Fellows who died in the past year. In addition to requesting that memoirs of Drs. William G. Spiller* and David Riesman be prepared, the Censors have asked that the following be mentioned.

Baxter L. Crawford, who died January 3rd, was elected a Fellow of the College in 1924. A graduate of the University College of Medicine, Richmond, Va. (1912), Crawford was assistant professor of pathology at the Jefferson Medical College, pathologist to the Jefferson Hospital and assistant visiting pathologist to the Philadelphia General Hospital. Unassuming in manner, but skilled in his specialty, he was a faithful supporter of and contributor to the Philadelphia Pathological Society, of which he was President, 1938 to 1940.

Walter Mendelson, a graduate of the College of Physicians and Surgeons of New York (1879), elected a Fellow in 1923, died January 19th. Keenly appreciative of the cultural aspects of medicine, Dr. Mendelson was especially interested in our Section on Medical History. His attendance and only too infrequent contributions there were thoroughly ap-

* The memoir of Dr. Spiller appears in the Dec., 1940 number of the *Transactions & Studies*.

preciated and will be correspondingly missed.

Daniel Mansfield Hoyt, a native of Florida, received his medical degree at the University of Pennsylvania (1901) and spent most of his career in this city. He was particularly concerned with tuberculosis and for the last several years of his life worked for the Veterans' Administration. He was elected a Fellow in 1908 and died in Florida on January 27th.

Samuel Horton Brown, Jr., elected a Fellow in 1916, died on June 12th. A graduate of the University of Pennsylvania Medical School (1899), he long specialized in ophthalmology, being on the staffs of several hospitals and a diplomate of the American Board. For the past 8 years he was active as Editor of the *Weekly Roster and Medical Digest*, which has prospered under his energetic management.

Charles Francis Nassau, a graduate of the University of Pennsylvania Medical School in 1891 and of Jefferson in 1906, was elected a Fellow in 1902. He was an able surgeon on the staffs of several Philadelphia hospitals, and clinical professor of surgery at Jefferson for a number of years. He was Director of Public Health of this city from January 1939 to the end of the same year. He died August 11th.

William Wilberforce Farr died August 19th. A graduate of the University of Pennsylvania Medical School (1887), he was an intern at the Germantown and Episcopal Hospitals of this city and one of the first residents at the newly founded Johns Hopkins Hospital. He was elected a Fellow in 1893. Having specialized for a time in nose and throat work, he had retired from practice some years before his death.

Joseph McIver, who was elected a Fellow in 1931, died September 7th, at Bryant, Texas, following an operation for appendicitis. Graduated from the University of Texas School of Medicine in 1912, Dr. McIver was chief resident physician at the Philadelphia General Hospital from 1913 to 1916, after which he specialized in neuropsychiatry. He served as instructor and associate in neurology at the University of Pennsylvania, as neurologist to several Philadelphia hospitals, to the House of Detention, and to the League Island Hospital during the World War. He was formerly president of the Philadelphia Neurological Society.

Arthur Caradoc Morgan, who was elected a Fellow of the College in 1918, died October 21st. A native Pennsylvanian, the son of Welsh parents, Dr. Morgan's energy found numerous profitable outlets. He taught for many years at his alma mater, the Medico-Chirurgical College, and at Temple University. He was on the Staff of the tuberculosis department at Blockley for 35 years. Deeply concerned with the affairs of organized medicine, he was President of the Philadelphia County Medical Society in 1925, and of the State Society, 1927–1928, was eleven times a member of the House of Delegates of the American Medical Association, and from 1931 to 1935 was an active member of the State Board of Medical Education and Licensure. "Spicey," as he was known to hosts of friends, was a ready speaker and writer; he was justly proud of his wide medical acquaintanceship and his unfailing ability to recollect personal names.

Pascal Brooke Bland, internationally known obstetrician, was elected a Fellow of the College in 1908 and died October 31st. He graduated from the Jefferson Medical College in 1901 as president of his class and was connected with that

school as an intern and in various staff positions till he became head of the department of obstetrics in 1925. He was elected emeritus professor in 1937. He was consulting obstetrician to several hospitals in this area, and author of numerous articles and three books on gynecology and obstetrics. A member of a number of American clubs and medical societies, Dr. Bland was also an associate fellow of the Royal Society of Medicine and a foreign corresponding member of the Royal Medical Society of Budapest. His knowledge of medical literature gained from his large and interesting collection of medical books of historical value made him a valuable member of our library committee.

Edward Browning Meigs, a graduate of the University of Pennsylvania School of Medicine (1904) elected a Fellow in 1911, was a scion of a distinguished medical family, all Fellows of this College. He was descended in direct line from Charles D., the celebrated obstetrician, John Forsyth, and Arthur V., President of the College from 1904 to 1907. Interested in fundamental problems of physiology, such as muscular contraction and the phenomenon of osmosis, Dr. Meigs was long the mainstay of the Society of Normal and Pathological Physiology, now the Philadelphia Physiological Society. He became a non-resident Fellow of the College in 1915, when he joined the Bureau of Dairy Industry of the United States Department of Agriculture, with which he was connected until his death on November 5th. In 1937 he was made chief of the division of nutrition and physiology there.

William Lawrence Estes, of Bethlehem, Pa., a native of Tennessee, a graduate of the University of Virginia Medical School (1877), and of the University of New York Medical Department (1878), was elected an Associate Fellow, as our Honorary Fellows were then called, in 1916. He was a member of the House of Delegates of the American Medical Association (1909) and was lecturer on physiology and hygiene at Lehigh (1883–1923). Long one of the prominent surgeons of eastern Pennsylvania, a member of the American Surgical Association and a Fellow of the American College of Surgeons, Dr. Estes was given the honorary degree of Doctor of Science by Lehigh University in 1934. He died October 20th.

Hans Zinsser, professor of bacteriology at Harvard, a bacteriologist of international repute, was elected an Honorary Fellow on May 10, 1937, when he gave one of the addresses at our Sesquicentennial celebration. He died on September 3rd of leukemia, the disease that killed the hero of his disguised autobiography, "*As I Remember Him.*" As he said of Francis Peabody: "in the manner of his facing death . . . its ugliness and cruelty were defeated." This is not the place to record the various details of Dr. Zinsser's distinguished professional career, or the many honors that were heaped upon him. Yet I would not want it to seem that I measure his importance as a scientist, as a popular writer for the laity and as a gifted musician, sportsman and individual by the brevity of this reference.

It is fitting to mention here also the death on October 26th of Mr. Charles Perry Fisher, for 50 years Librarian of the College till his retirement in 1932. During his incumbency, and in no small measure due to his devoted services, our Library rose from a collection of some 25,000 volumes to its present position as one of the most important medical libraries in the country.

Annual Report on the Library*

Our annual reports in recent years have attempted to lift one by one the veils which clothe in mystery the library's articulation. We have already reviewed, for instance, the broad terrain on which a large medical library must keep a watchful eye (1938), and something of the professional tasks of the library assistants (1939). We have once or twice hinted that money was involved in the library's operations, and now we propose to raise the veil that covers this kinetic joint.

Within a few months after the library was started, in 1788, by Dr. John Morgan's first donation of books, the College adopted a proposal that " . . . as soon as the treasurer has made his annual report of the balance remaining in his hands, the college do grant such sums as they may think proper for the service of the library for the ensuing year." An annual appropriation is still being made, though it has by now dwindled from the status of paternal total support to what might be regarded as merely a slight token of esteem, were the general finances of the College sufficient to afford a more liberal dispensation. The College also contributes to the support of the library, it should be added, by paying the salary of the librarian, who has, however, other College duties, not essentially connected with the library, entrusted to him. Fortunately, the library, though it still needs the College's appropriation, is largely self-supported, as it were, thanks to a number of endowed funds created in the last 70-odd years specifically for its benefit.

There are at present 41 invested library funds. The oldest of these originated in a gift of $445.90 from the Philadelphia Medical Society on its dissolution in 1868 after an existence of 79 years; this gift was specifically designated "to increase the library of the college." The institution of the forty-first fund, the "Fund of the Friends of George E. Pfahler", was a notable library-event of the current year. The principal amounts to $3,000 (the original gift of $1,000 from the friends of Dr. Pfahler was first doubled and then trebled by the distinguished Fellow in whose honor the fund was instituted), the income from which is to be devoted to the purchase of radiological and roentgenological literature.

These 41 funds yielded an annual income of approximately $19,000. The fact that 26 of the funds are restricted to the purchase of books and periodicals (ten of them, furthermore, to those in specific fields) would raise an almost insurmountable problem, if the other 15 funds did not number among them the largest one of all—the Louis A. Duhring Fund, "for general purposes", which yields an income of approximately $11,850. As the other unrestricted funds yield a total income of no more than a third of that amount, one can easily see that, without this magnificent bequest, the library might be a splendid tomb for unknown and inaccessible treasures.

The possessions of a library would be futile indeed, were there not available an adequate staff of persons trained to make them accessible and usable. The expenditure of approximately $9,400 in

* October 16, 1939–October 15, 1940.

salaries for these indispensable midwives and middlemen (seven full-time, and two part-time, assistants) can, therefore, scarcely be thought an extravagance. The truth is, that the Library Committee, fully conscious of the library public's very real dependence on the library staff, regrets each year its inability to recompense more fittingly the vital, skillful services of these assistants. It is no easy matter for a committee with a conscience and a limited budget to draw the financial line of demarcation between matériel and personnel.

Under normal conditions, about $6,000 is expended annually on subscriptions to periodicals; about $2,000 on the purchase of books; about $2,000 on binding; and about $500 on supplies. In the past year, of course, the epidemic of wars has played havoc with the regular receipt of, and payment for, periodicals from the nations directly and obliquely involved in the wars. The handling of most of our English and continental subscriptions had been entrusted to a Netherlands and an Italian agent. Payments have been made on some subscriptions which have not materialized at all. On some subscriptions which have been partially fulfilled, payments have not been made, both because complete fulfilment seems dubious and because the agents themselves have pointed the way to a waiting policy. Our current-periodicals department is endeavoring to re-adjust matters so that subscriptions may be paid directly to publishers, wherever regular contact with them seems reasonably assured, and, where it cannot, so that copies of the periodicals are collected and held for us against the arrival of a happier day. In this endeavor we have found our agents entirely ready to co-operate, as far as lies in their power. The library reports issued during the war years 1914–18 seem, in this respect, singularly applicable to our present situation. We of the library see, almost daily, evidences of that catastrophe in our working collections. It is tragic and almost beyond belief, that within the same generation the experience must be repeated. But this is our relatively small share in the all-encompassing misfortune; needless to say, we shall do what we can to minimize the ultimate damage in our bailiwick.

This year our expenditures for binding exceeded the normal by about $500. Assistants engaged especially to check our periodicals for inclusion of our holdings in the forthcoming revised edition of the *Union List of Serials* turned up a great number of worthy candidates for binding: (1) volumes that had been completed only long after the year of publication; (2) seemingly incomplete volumes that we learned from the *Union List* were complete, in the sense that no further numbers were published. In this way we have saved from greater probability of damage or loss some hundreds of important volumes. The annual appropriation from the College obviously helps considerably to make possible such constantly occurring out-of-course expenditures as this.

One fourth of the endowed funds are restricted, as we have said, to the purchase of books, or books and periodicals, in specific fields of medicine. Certain other funds *exclude* expenditures for books or periodicals. Still others, while they do not restrict purchases to specific fields, prohibit expenditures for anything but books and periodicals. Thus, the restrictions form a rather complicated pattern. The question of pooling these funds arises from time to time, and there can be no doubt that one result of so doing would be greatly to simplify our problem in 'funding' the bills. Two

objections, however, invariably present themselves, one of which seems almost insurmountable—the expenditure of time and money that would be required to have legally set aside the many restrictions governing the funds. The other is more easily answered: the praiseworthy desire to have a fund serve as a memorial could be satisfied almost as well as it is at present by the creation of a new bookplate containing the names of all the funds contributing to the common fund. As things are, the restrictions demand that the complicated business of 'funding' the bills, supposedly a financial transaction, be performed by some one familiar with foreign languages and with the language of medicine; and so this task, requiring considerable financial agility as well, is entrusted to our current-periodicals department. As a common fund would, from all practical points of view, be a more efficient method of handling the library's finances, it seems possible to believe that the obstacles which stand in the way of its creation will eventually yield somehow to the logic of efficiency.

The salaries of the assistants are assigned to the so-called Library General Account, composed of the funds (including the Duhring) left for general purposes, and the College's appropriation. Expenditures for binding and supplies are likewise assigned to this account or to funds which exclude the purchase of books and periodicals. Periodicals, the expenditures for which are fairly well determined a year in advance, are as far as possible assigned from year to year to a fund whose specifications they meet, or to a given general book-and-periodical fund. One minor 'paper' disadvantage in this practice is that, when, as has happened in the past year or two, a restricted fund 'folds up', either temporarily or permanently, periodicals which have long been identified with a given sponsor become orphans of the storm and the continuity of association is broken. Other factors which complicate the funding of the periodicals, and the first of which precludes an exact estimate of the expenditures for periodicals in advance, are the common European custom of varying the price per issue, and the non-uniform starting dates of the volumes. The funder's life would unquestionably be a happier one if all periodicals had a fixed annual price and if all began and concluded their volumes at the same time. But not even a world of dictatorships could bring this to pass, in all probability, and the administration of the periodical in which this report appears would doubtless be in the front line of protestants against any attempt to bring about the latter form of regimentation! Books, of course, are assigned whenever possible to an appropriate restricted fund; when none is available, to the Library General Account.

The Library Committee receives from the clerk of the College a monthly (except during the summer) statement showing the balances on hand at the time of the last committee meeting, the incomes received since then, and the expenditures (authorized by the committee at its last meeting), and, finally, the balances on hand at the time of the current meeting, when they receive also a new package of funded bills to be approved. Inasmuch as the clerk's report is not received until a few moments before the meeting, these bills have been funded on the basis of balances shown on the preceding report, minus the expenditures authorized at that meeting, and, except in rare instances, without regard to anticipated incomes. Thus, the committee receives no bill which is not covered by an ade-

quate balance in the fund to which it is assigned; and the untouched incomes on the current report serve as a guide, when referred to known obligations, to the amount available for new expenditures. Owing to the vagaries of investments, the monthly incomes do not remain constant from year to year, nor, of course, can even the annual incomes be precisely determined in advance. For that reason, we attempt to have available a reserve sufficient to offset fluctuations and loss. There are times, we must confess, when one or another fund may show a handsome balance of one cent, and that achieved not without toil and tears; but, except in one or two instances when very slight errors in figuring have been made, our financial reports of the past half-dozen years have appeared unrubricated. This we owe to the wizardry of those who have this miracle regularly to perform.

Despite this large measure of financial autonomy, the library, as all other departments of the College, remains in fact as in principle close under the wing of the Council of the College. The chairman of the Library Committee, and the Honorary Librarian, are members of that body, of course, and no major change in policy, such as the recent opening of the library on Sunday afternoons, could conceivably be effected without its approval. The library's relatively independent financial status serves, in effect, merely to ease the College's position with respect to the maintenance of what is perhaps its greatest contribution to the community. But it is now clear, we hope, how great a debt the Fellows and other beneficiaries of the library owe to the donors of the 41 funds which constitute the library's life-lines; clear, also, that these funds, which allow us to mark time, as it were, do not provide for development further of present holdings or services; for the acquisition of new ones; for a scale of remuneration to the library staff consonant with their importance to the scheme as a whole. In the setting forth of things as they are, we keep ever in the mind's eye a vision of them as they might be, if this fundamental joint were better lubricated.

Inventory

	1940	1939	1940	1939
Total number of accessioned items[1]			154,822	152,454
Incunabula	411	410		
Manuscripts	538	536		
Other items[2]	153,873	151,508		
	154,822	152,454		
Total number of unaccessioned items[3]			319,858	316,208
Reports and Transactions	25,594	25,530		
Periodicals "reserve"[4]	4,636	4,614		
More or less complete volumes of other periodicals not regularly received	2,975	2,988		
Theses and Dissertations	47,026	45,992		
Pamphlets (less than 100 pages)	239,627	237,084		
	319,858	316,208		
Total number of current periodical publications regularly received			1,134	1,202
Duplicate books			13,612	13,100
Portraits[5]			46,943	39,938

Distribution of this Material

	Accessioned items	Unaccessioned items
General Library (including the Lewis Library)	150,607	319,854
On permanent deposit:		
Gross Library	3,799	4
Parry Library of the Obstetrical Society of Philadelphia	217	0
Mütter Museum[6]	199	0
	154,822	319,858

[1] An accessioned item may be any kind of graphic material that is kept within covers, whether these be made commercially or in the library, of paper or of more durable material. The accessioned item might comprise, for instance, part of a book, or one or more books; a part of a periodical volume, or one or more complete periodical volumes; reports, pamphlets, or theses, single or collected; an atlas or photograph album.

[2] Including 37 'rare' books acquired during the year.

[3] While the accessioned items contain some material in paper covers, it should be noted that most Reports and Transactions, pamphlets, and theses, also paper covered, are not accessioned, but that all might be at any time, if any intrinsic reason for so doing should present itself.

[4] More or less complete duplicate volumes of important and much-used periodicals.

[5] Including 105 oil and 456 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

[6] The books of the Mütter Museum are not permitted to be removed from the College building.

Current Periodicals

Total number of periodicals regularly received in the library: 1,134 titles

	Purchase	*Exchange*	*Gratis*	*Annuals & 'Books'*	*Total*
American (United States)	146	66	160	44	416
Australia and New Zealand	1	4	2	0	7
Belgium*	15	6	1	0	22
British Isles	71	17	5	6	99
Canada	1	6	6	2	15
Ceylon and India	2	5	1	1	9
Cuba and Puerto Rico	0	7	7	0	14
France and Colonies*	97	12	6	4	119
Germany*	151	0	0	11	162
Italy*	78	21	6	0	105
Japan, Korea, Manchoukuo	5	14	3	3	25
Mexico and Guatemala	0	5	5	0	10
Netherlands and East Indies	9	1	2	1	13
Russia	3	5	1	0	9
Scandinavia* (Denmark, Norway, Sweden)	12	4	0	1	17
South America	4	20	16	2	42
Switzerland*	20	2	3	0	25
Miscellaneous†	4	13	6	2	25
Totals, 1940	619	208	230	77	1,134
(Annuals & 'Books')	26	22	29	77	
Grand Totals, 1940	645	230	259		1,134
Grand Totals, 1939	688	248	266	[105]	1,202

* Probably a large number of the Belgian and French journals counted above have, at least temporarily, suspended publication, though we have had no notification of this; and the same remark may apply to the German, Italian, Scandinavian, and Swiss periodicals. They are included in the report because issues were

being received through our agent in the Netherlands until May, when shipments ceased. (Since late October, however, after the period covered by this report, these shipments have recommenced, on a limited scale; and many issues published in the spring or summer are finally being received, thanks to a new shipping arrangement through Lisbon.)

† Fewer than 6 journals each from: British Africa, China, Czechoslovakia, Egypt, Jugoslavia, Lithuania, Palestine, Philippines, Roumania, Siam.

These figures give the number of only those publications whose receipt may be considered "regular", though scarcely "current", considering the uncertain circumstances of foreign publication and transatlantic mailing since May and June, 1940. Of 78 journals included in the census a year ago but omitted from the present report, only 18 are positively known to have ceased (or temporarily suspended) publication—comprising chiefly British, French, and Polish besides American journals; but the same is almost certainly true of many others about which no information has yet been received. Another group of some 40 publications issued not more than once annually, and not received during the past 12 months ending October 15, is omitted from the census. One or more numbers of 159 other journals, also not included in the tabulation, were added to the files, scattered issues (current or otherwise) having been received by donation.

New titles: Of the 39 publications added to our list during the year, 8 are received by purchase; 4, by exchange; 27, gratis. Twenty-seven of these are journals which have recently begun publication (1936–40) and are now on file from the first number issued.

Separate issues received and filed: 11,944 (exclusive of duplicates, 4,699, and of reserves, 803)—a total about 2,500 fewer than the year before, as a result of the European situation. Of the total number, 2,530 were scattered issues received from Fellows and other donors; and 85 others were previously-lacking back-numbers supplied by publishers or editors in response to claims, completing 40 volumes.

Back files of 5 publications were acquired: 22 complete volumes (12 purchased, 10 gratis).

Visitors to the Current-periodicals Room during the year were recorded to the number of 6,760—an increase of 40 over the number for the preceding year. Of this year's total, some 1,170 were visitors during the 76 evenings the library was open (170 persons fewer than the year before); and 185 were visitors on 18 Sunday afternoons.

Readers' Use of the Library

Library hours: the library was regularly open daily, except Sunday, from 9 to 6; on Wednesday and Friday evenings until 9:30; on Sunday afternoons from 2 to 5:30 (January 7 to April 28, 1940, incl.; October 6 and 13). From June 10 to September 7, incl., the library was open Mondays to Fridays, incl., from 9 to 4, and closed on Saturdays and Sundays. The library was closed, as usual, on the following legal holidays: Thanksgiving, Christmas, New Year's, Memorial, Independence, and Labor days.

			Non-Fellows		*Fellows*		*Totals*	
	1940	*1939*	*1940*	*1939*	*1940*	*1939*	*1940*	*1939*
Number of visitors:								
Days	(294)	(293)	9,130	8,963	2,026	2,063	11,156	11,026
Evenings	(76)	(78)	1,634	1,516	225	204	1,859	1,720
Sundays	(18)		443	—	27	—	470	—
			11,207	10,479	2,278	2,267	13,485	12,746

	1940	*1939*
Circulation of books:		
Number of volumes taken out	8,379	8,524
(Books: 3,929; Periodicals: 4,450)		
Number of volumes consulted in the library	50,520	49,725
(Books: before 1700, 203; before 1850, 850; after 1850, 13,452)		
(Periodicals: before 1850, 349; before 1899, 1,574; after 1899, 34,092)		

The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and works of reference kept on the

shelves in the Reading Room; the Fellows of the College, and occasionally others by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

Inter-library Loans: The library has sent 117 (1939: 111) volumes on inter-library loan to 25 (1939: 19) libraries in 12 (1939: 11) States, and has borrowed 19 (1939: 21) volumes from 5 (1939: 2) libraries. The Philadelphia Union Library Catalogue has undoubtedly contributed to the geographically-more-wide-spread calls on us for this service. There were, as happens each year, a number of requests we could not fill: 14 volumes asked for we did not have; 5 are on the restricted list; 2 requests were for current, unbound journals. Our photostat answered the need in some of these cases, and in many more a knowledge of this service obviously forestalled a request for loan of a volume. Our borrowings were chiefly from the Army Medical Library and the library of the New York Academy of Medicine, but the Library of Congress, the Boston Public Library, and the library of the University of Michigan also graciously answered requests for loans.

Use of the study rooms: Number of volumes used in these rooms during the year: 945 (1939: 1,450).

Photostats: 917 photostatic prints have been furnished to Fellows (1939: 715); 553 prints to non-Fellows (1939: 702); 930 prints to the library. The last include a copy of an incunabulum (bringing the total of photostated incunabula to 315), portraits, rare books on loan, etc.

Acquisitions and Accessions

Received from all sources:

1940: 3,118 volumes (including the bound and accessioned volumes of periodicals, 99 unbound reports and 651 duplicates); 3,137 pamphlets; 2,381 theses; 21,525 numbers of various journals.

1939: 3,992 volumes (including the bound and accessioned volumes of periodicals, 188 unbound reports and 1,383 duplicates); 2,792 pamphlets; 8,018 theses; 21,424 numbers of various journals.

Accessions:

1940: 2,368 volumes (978 by purchase; 701 by gift; 689 by exchange).
(Books, 702; Periodicals, 1,666).

1939: 2,421 volumes (1,136 by purchase; 824 by gift; 461 by exchange).
(Books, 1,050; Periodicals, 1,371).

Donations

The individual donors for the past year number 290 (1939: 300).

The library is indebted for large gifts of books, pamphlets and unbound periodicals to the following donors:

P. Blakiston's Son & Co.; Drs. C. W. Burr, Burton Chance; Estate of Dr. C. N. Davis; Drs. A. A. Eshner, C. B. Farr; Mrs. G. Fetteroff; Drs. T. S. Githens, S. S. Greenbaum, J. P. C. Griffith; Hahnemann Medical College Library; Drs. S. McC. Hamill, R. J. Hunter, E. B. Krumbhaar; Lea & Febiger; Drs. B. B. V. Lyon, J. F. McCahey, Joseph McFarland; Medical Library Association Exchange; Drs. C. C. Norris, R. F. Ridpath; W. B. Saunders Co.; Drs. A. C. Sautter, J. D. Seiberling; University of Pennsylvania Library; Drs. Erich Urbach, Joseph Walsh, P. F. Williams, A. C. Wood; Mrs. H. C. Wood, 3rd; John Wyeth & Brother, Inc.

Various publishing houses have presented volumes as follows: P. Blakiston's Son & Co., 23; F. A. Davis Co., 14; Lea & Febiger, 34; J. B. Lippincott Co., 15; W. B. Saunders Co., 60.

Twenty-two volumes were presented by the following authors or editors: J. P. Arcieri, J. Beardwood, Jr., & H. T. Kelly, F. Beekman, W. R. Hill & D. M. Pillsbury, L. A. Julianelle, Lahey Clinic of Boston, Council on Medical Education of the A. M. A., Nu Sigma Nu, H. K. Pancoast, E. P. Pendergrass & J. P. Schaeffer, Pan American Sanitary Bureau, J. L. Rice, S. I. Meredith, H. W. Smith, L. W. Smith, Edward Weiss & collaborators, W. L. C. Spaeth et al., J. P. Vieira, J. C. Yaskin.

Two books were sent from the publishers at the request of the following authors: H. W. Dargeon and W. G. Leaman.

Exchanges

The *Transactions & Studies* was sent, either as gift or in exchange for 302 other serial publications, to 337 organizations.

One distribution (one unbound journal) has been made through the Medical Library Association Exchange. The library has received thirty such distributions.

Theses and dissertations to the number of 1,610 have been received from the following European

Schools of Medicine with which we exchange publications at the present time: Universities of Amsterdam, Bern, Geneva, Köln, Lausanne, Leiden, Paris, Tartu.

Work of the Cataloguers

	1940	*1939*
Number of works classified, shelf-listed, and for which cards were filed	555	929
Cards typewritten, examined and filed	12,189	8,647
Other cards altered and filed	11,402	10,341
Pamphlets and reprints subject-headed and arranged alphabetically by subject, and by author under the subject	1,788	1,825

Miscellaneous Notes

Exhibits. The death of Dr. Harvey Cushing was an occasion for sorrow in the library, because he had been one of its friends and benefactors for many years. Our copy of the very rare *Epitome* of Vesalius' *Fabrica*, for instance, was his gift. The library, therefore, felt it quite fitting to prepare a comprehensive exhibit of his publications, to which were added some characteristic letters and other memorabilia of a personal sort. An exhibit also was held of the medical portrait-etchings and original anatomical illustrations of the late Erwin Faber, a large collection of which had recently been given to the library through the good offices of Dr. Balduin Lucké and Dr. Samuel B. Sturgis. For the University of Pennsylvania's Bicentennial Celebration the library brought out what is perhaps its greatest collection of material on a single individual, its Harveiana.

Rariora. Dr. Charles W. Burr enabled us, with his characteristic generosity, to add two volumes to the collection of incunabula: Robert Duval's *Compendium memorandorum Plinii*, Paris, 1500; and Girolamo Manfredi's *Tractatus de peste*, Bologna, ca. 1482. Another notable acquisition was the gift, from the Philadelphia Academy of Surgery, of Paré's *Cinque livres*, the preface of which was reprinted, with a translation, in the April, 1940, number of this publication.

Collection of medical art. The library has long had a splendid collection of medical art (we use the term to describe all types of graphic art applied to medical subjects), but it has been ill-assembled and ill-catalogued from the point of view of use for research. The library has been fortunate (through the mediation of Dr. E. B. Krumbhaar, president of the College) in enlisting as active Director of the collection Dr. Samuel B. Sturgis, a Fellow who has made important additions to the collection. Dr. Sturgis has already mounted hundreds of the prints and provided suitable albums to contain them. His plans envisage the assembling also of examples of the originals of anatomic illustrations made for books and articles, so that there will be available eventually an unusual collection of source material for the study of the technique of illustration in various periods, of anatomic concepts, and of characteristic work of individual artists. Needless to say, the project includes the preparation of such indexes as will be necessary for research purposes.

Advisory Committee. The Library Committee and the librarian have for some years felt that a judicious selection of publications for purchase demanded more varieties of specialized knowledge than their small group could be expected to provide. In the past year, therefore, a number of specialists was invited to act as an unofficial advisory committee on purchases, and it is believed that the advantages of this policy will be in-

creasingly reflected in the quality of the library's acquisitions.

Sunday openings. In January the library took another step forward in the expansion of its services, and thereby proved again that adventure can create demand. Acting under no pressure, but only in the belief that many of the younger physicians and the students would welcome the opportunity of coming to the library on Sunday afternoons, we started a trial period of Sunday afternoon openings on January 7. From the first afternoon on, the attendance has amply justified the venture, and the library will, as a consequence, now regularly maintain this opening during the academic year.

Dr. Riesman. The library sustained, in June, a very great loss in the death of the Honorary Librarian, Dr. David Riesman. As a member of the Library Committee since 1932, as its chairman for several years, and finally as the Honorary Librarian, Dr. Riesman brought to these responsibilities, which he seemed particularly to cherish, a rare combination of qualities: learning, faithfulness, enthusiasm, vision. The sound of his quick, eager step on the hard floor as he came through the Reading Room has joined too soon the inaudible, but still-felt, echos of the other great men who contributed in fundamental ways to the development of this library.

The Staff. The librarian contributed an article or two to various publications, including the *Transactions & Studies.* He continued to serve as editor of the last, and as superintendent of the College. With two exceptions, the corps of assistants remained unchanged, comprising the following: Miss Gertrude Bishop, cataloguer; Miss Sallie H. Todd, assistant cataloguer; Miss Helen Jackson, assistant in charge of the Reading Room; Mr. R. H. Baugh, assistant in charge of the Current-periodicals Room; Miss Kathryn Haegele, junior assistant, and substitute assistant in the Reading Room; Miss Marion Jackson, junior assistant and photostat operator; Miss Hertha Bishop, junior assistant in charge of book-orders. Mrs. H. C. Wood, 3d, part-time assistant, resigned as of April 1 and was succeeded by Mrs. Curt Lundquist. John Jackson, a student at the University of Pennsylvania, began as part-time junior assistant on October 6.

W. B. McDaniel, 2d,
Librarian

Approved:
William Egbert Robertson, M.D.,
Chairman

Reports of the Committees on the Mütter Museum and College Collections

The Museum

The Museum was open, on days when the College building was open, from 10 to 1, and from 2 to 6, except Saturdays, when the hours were from 10 to 1. During these hours, the clerk-technician, Mrs. Wade, was constantly in attendance, and the curator, Dr. McFarland, was often present, also. In addition, the Museum was open on the evenings of the Stated Meetings of the College and during the evening Lectures for the General Public, the clerk-technician being in attendance at those times. At the request of some of the Sections of the College, the Museum was opened for an hour or so before certain of their meetings.

More than 1000 visitors registered during the year. There were, of course, many more who failed to sign the register. The increased number of visitors, Fellows and others, would appear to indicate a growing interest in the Museum. This is, in large measure, due to the courtesy and constant attendance of the clerk-technician.

The Thomas Dent Mütter Lecture LII was given by Dr. Howard T. Karsner, who spoke on "Certain Ovarian Tumors Associated with Sexual Endocrine Dysfunction."*

One volume of the new Accessions Catalogue of the Collections of the Museum was completed during the year, and a second volume is now in preparation. This catalogue will contain interesting records of each item, so far as data are available, associating many of the specimens with prominent members of the College, past and present.

Certain of the collections were used for teaching purposes, as in the past, by some of the medical schools of the city.

A considerable number of objects from the storeroom, including wet specimens, fractured and diseased bones, models, and instruments, were labeled and catalogued and placed on display. A number of specimens requiring attention were repaired.

Dr. Joseph McFarland was re-appointed curator for the year 1940–41, and Mrs. Ella N. Wade was appointed clerk-technician for the year 1940–41.

Accessions to the permanent collection of the Museum during the year, and subject to the Mütter deed of gift, were as follows:

(1) A case of instruments, labeled as follows: "Captured and brought from Metz. A. Vernon Haig, A. E. F. 1917." Presented by Hubley R. Owen, M.D.

(2) Five plaster sections of the thorax and abdomen; nine rodent skulls; two white-tailed jackrabbit skulls; one red squirrel skull; three gray squirrel skulls; three muskrat skulls. Presented by William Egbert Robertson, M.D.

(3) Two lancets, formerly the property of Judge Rankin, Lebanon Co., Pa. Presented by his grandson, C. R. Rankin.

(4) Framed photograph of the Execution of Ling Chee, or the cuts of 1000 knives. (This was the punishment for patricide in China about 1890. Photo-

* Printed in the *Transactions & Studies*, 4 ser., vol. 7, no. 4 (Feb., 1940), pp. 301–341.

graph was taken by the first officer of the Fat Chan River boat.) Presented by Charles D. Hart, M.D.

J. PARSONS SCHAEFFER, M.D.
Chairman

COLLEGE COLLECTIONS

DURING the year, the curator and the clerk-technician completed a new catalogue of the College collections under the care of this committee. This is now available for general reference.

In addition to those noted in the June, 1940, number of the *Transactions & Studies*, accessions have been as follows:

(1) Medal bearing the portrait of Dr. Frederick Banting. (Canadian National Exhibition. Toronto, 1923.) Presented by Jabez H. Elliott, M.D., through E. B. Krumbhaar, M.D.

(2) One large University of Pennsylvania Bicentennial medal, and seven smaller ones in the form of badges. Presented by the Bicentennial Committee, University of Pennsylvania.

(3) Oil portrait of William Zentmayer, M.D., painted by Daniel Garber. Presented by the College's Section on Ophthalmology.

J. PARSONS SCHAEFFER, M.D.
Chairman

Reports of the Treasurer for the Year Ended November 30, 1940

BALANCE SHEET

Assets			
Plant			
Land at 22d & Ludlow Sts.	$46,409.75		
Building at this address	364,681.41	$411,091.16	
Other Real Estate			
Land at 13th & Locust Sts.		150,000.00	
Fund Investments			
Stocks, Bonds, Mortgages and Real Estate Received in Foreclosure		658,207.61	
Income Invested in Bonds		4,913.88	
Accounts Receivable		225.28	
Notes Receivable		300.00	
Cash			
Trust Funds			
Principal Account for Investment	22,764.72		
Income	10,013.34		
Administration	7,873.20	40,651.26	
Total			$1,265,389.19
Liabilities			
Unexpended Appropriations			
Library General Account	2,674.13		
Publication Committee	339.20		
Contributions for Furnishing President's Room	525.00		3,538.33
			$1,261,850.86
Plant Funds Invested in Land and Building		$561,091.16	
College Funds			
Library Funds	440,618.76		
Publication Funds	16,282.73		
Prize and Lecture Funds	32,596.32		
General Operating Funds	176,489.61		
Entertainment Funds	12,072.07		
Miscellaneous Funds	10,024.99	688,084.48	
Unexpended Income from Funds for Special Purposes		10,013.34	
Unexpended Current Operating Income		2,661.88	
			$1,261,850.86

CASH STATEMENT, NOVEMBER 30, 1940

Receipts		
Balance on hand 12-1-39		$14,020.40
Gifts for designated purposes		
Friends of Dr. George E. Pfahler	1,000.00	
Dr. George E. Pfahler	2,000.00	3,000.00
Investments matured or sold		67,542.17
Accretions to Principal from sale of above securities		2,837.25
Income transferred to Principal		1,329.44
Pledges paid to Reserve Fund		20.00
Entrance Contributions to Reserve Fund		590.00
Contributions from Fellows		18,813.00
Contributions for use of Halls		1,205.00
Contributions for use of Lantern		241.00
Contributions to the Library		806.50
Contributions to Entertainment Committee		50.00
Rent from Property 13th & Locust Sts.		5,937.50
Dividends from Insurance		225.00
Interest on Western Savings Account		68.42
Interest on Notes Receivable		20.00
Notes Receivable		200.00
Income from Special Funds		29,770.01
Income from Library		995.57
Miscellaneous Income		141.79
Total		$147,813.05
Less Total Disbursements		107,161.79
Balance on hand November 30, 1940		$40,651.26
Penna. Company Principal Account		22,764.72
Penna. Company Income Account		14,846.47
Western Savings Fund Account		3,001.71
Petty Cash Account		38.36
Total Cash Balance		$40,651.26

Disbursements	
Securities Purchased	$52,346.77
Committee on College Collections	428.00
Committee on Publication	1,871.19
Committee on Entertainments	577.50
Hall Committee	11,542.42
Secretary	2,329.77
Treasurer	9,956.69
Library Committee	24,474.44
Miscellaneous Disbursements	3,634.90
Total Disbursements	$107,161.79
Principal Account for Investment	$22,764.72
Trust Fund Income Account	10,013.34
Administration	7,873.20
Total	$40,651.26

SUMMARY OF OPERATING INCOME AND EXPENDITURES, 1940

Balance on hand 12-1-39		$1,693.41	
Income			
Contributions from Fellows	$18,813.00		
Contributions for use of Halls	1,205.00		
Contributions for use of Lantern	241.00		
Rent Property 13th & Locust Sts.	5,937.50		
Insurance Dividends	225.00		
Interest on Western Savings Fund Account	68.42		
Income from Funds for General Operating Purposes	7,452.09	33,942.01	
Total			$35,635.42
Expenditures			
Library Committee		7,600.00	
Hall Committee		11,489.95	
Treasurer		9,955.41	
Secretary		2,329.77	
Publication Committee		1,170.41	
Committee on College Collections		428.00	32,973.54
Unexpended Operating Income			$2,661.88

SUMMARY OF COLLEGE TRUST FUNDS

	Principal	Investment	Balance of Income (1939)	Income	Expenditures	Balance of Income (1940)
Library Funds	$440,618.76	$420,013.14	$2,762.06	$18,754.93	$16,956.82	$4,560.17
Publication Funds	16,282.73	16,316.56		653.52	653.52	
Prize and Lectureship Funds	32,596.32	32,414.33	3,379.69	1,022.99	1,771.23	2,631.45
General Operating Funds	176,489.61	175,559.00	(57.55)	8,100.03	8,042.48	
Entertainment Funds	12,072.07	12,030.18	(837.06)	816.04	725.81	(746.83)
Miscellaneous Funds	10,024.99	6,788.28	3,126.05	442.50		3,568.55
	$688,084.48	$663,121.49	$8,373.19	$29,790.01	$28,149.86	$10,013.34

	Principal	Investment	Balance of Income (1939)	Income	Expenditures	Balance of Income (1940)
Library Funds						
Baker, Henrietta R. F.	$5,412.06	$5,378.61	$21.79	$265.00	$132.26	$154.53
Bent, Luther S.	1,064.00	1,042.55	12.01	44.81	33.38	23.44
Binding Books, Periodicals, etc.	420.00	401.37		22.34	22.34	
Carter, Wm. T.	5,000.00	4,966.88	83.21	157.50	157.13	83.58
Catalogue Endowment	1,032.32	1,024.35		31.50	31.50	
Clarkson, Gerardus	1,000.00	967.50	10.83	10.00	13.92	6.91
Dereum, Francis X.	5,000.00	4,993.50	91.02	144.50	136.15	99.37
Duhring, Louis A. (Book)	5,006.25	4,998.81	132.12	242.50	163.18	211.44
Duhring, Louis A. (Library)	260,361.63	253,009.57		11,640.82	11,640.82	
Eshner, Augustus A.	5,000.00	5,000.00	131.17	300.00	224.84	206.33
Friends of Library #2	361.29	360.00	26.10	9.00		35.10
Friends of George E. Pfahler	3,000.00	2,929.25		20.00	8.78	11.22
Griscom, John D.	3,250.00	3,337.50	73.70	250.00	249.86	73.84
Gross, Samuel D.	2,910.00	2,859.75	630.13		75.00	555.13
Harte, Richard H.	5,187.48	4,705.77	75.19	359.98	189.29	245.88
Hunter, Charles T.	489.73	454.19	6.43	3.00	2.63	6.80
Rare Book	475.00	451.20	57.00	19.00	25.00	51.00
Jenks, William F.	7,026.56	7,033.54	109.92	254.50	149.13	215.29
Judson, Oliver A.	1,139.91	1,138.84	13.91	51.20	40.06	25.05
Keating, Wm. V. and John M.	1,064.00	1,033.18	21.92	44.81	29.80	36.93
Keen, William W.	5,525.55	5,523.24	49.63	215.36	138.23	126.76
Leffman, Henry			147.90	410.12	447.12	110.90

Library Endowment	14,908.25	14,864.98	63.56	330.48	178.30	215.74
Longstreth, Morris	23,559.54	14,314.78		662.22	662.22	
Magee, Horace	15,631.06	15,793.89	61.40	513.15	282.03	292.52
Mears, J. Ewing	5,411.87	5,392.80	13.37	258.00	180.07	91.30
Mills, Charles K.	182.71	161.30	3.83	2.00		5.83
Mitchell, S. Weir	5,144.90	5,090.76	100.25	234.70	160.53	174.42
Montgomery, E. E.	3,178.75	2,016.02	24.54	149.17	46.87	126.84
Musser, John H.	518.59	500.00	14.92	22.50	21.50	15.92
Newcomet, Elizabeth K.			72.40	47.50	70.59	49.31
Norris, William F.	4,593.07	4,621.39	38.43	213.46	121.00	130.89
Oliver, Charles A.	1,270.65	1,222.45	.08	50.00	18.72	31.36
Phila. Medical Society	557.50	570.25	25.24	27.00	27.28	24.96
Rodman, Lewis	5,074.64	5,058.90	37.48	149.50	84.63	102.35
Vinton, Charles H.	11,209.22	9,904.53	232.85	522.28	442.38	312.75
Warren, Douglas Stockton	3,000.70	2,910.00	55.86	124.00	104.33	75.53
Weightman, John F.	1,193.70	1,122.65	5.85	50.32	25.71	30.46
White, J. William	5,242.31	5,178.16	140.89	251.00	218.43	173.46
Wistar, Caspar	5,263.53	5,241.02	55.52	244.68	138.00	162.20
Wood, George B.	9,953.99	9,458.16	120.63	407.03	263.81	263.85
Ziegler, S. Lewis	5,000.00	4,981.50	.98			.98
	$440,618.76	$420,013.14	$2,762.06	$18,754.93	$16,956.82	$4,560.17

SUMMARY OF COLLEGE TRUST FUNDS—*Concluded*

	Principal	Investment	Balance of Income (1939)	Income	Expenditures	Balance of Income (1940)
Publication Funds						
Da Costa, J. M.	$4,766.05	$4,801.04		$188.76	$188.76	
Davis, G. G.	491.87	491.87		22.50	22.50	
General Publication	2,067.54	2,068.84		94.70	94.70	
Lister International Medical Congress	2,009.78	1,957.67		45.50	45.50	
Meigs, Arthur V.	1,034.50	1,000.00		50.00	50.00	
Tyson, James	528.99	498.50		22.50	22.50	
Wyeth, Francis Houston	5,384.00	5,497.84		229.56	229.56	
	$16,282.73	$16,316.56		$653.52	$653.52	
Prize and Lectureship Funds						
Alvarenga Prize Fund	$9,658.33	$9,468.91	$1,009.57	$224.99	$250.00	$984.56
Anders, James M., Lectureship Fund	6,002.99	5,993.79	1,081.89	288.00	84.00	1,285.89
Newbold, Mary Scott, Lectureship Fund	17,025.00	16,951.63	1,288.23	510.00	1,437.23	361.00
	$32,596.32	$32,414.33	$3,379.69	$1,022.99	$1,771.23	$2,631.45
General Operating Funds						
Clarkson, Samuel	$3,000.00	$3,011.61	($57.55)	$142.50	$84.95	
College Endowment	14,817.92	14,834.24		649.74	649.74	
Lea, Carolyn Tyler and Arthur H.	50,204.00	50,231.59		2,455.03	2,455.03	
Reserve	54,376.93	53,296.67		1,892.81	1,892.81	
Shippen, Elizabeth	5,109.73	5,107.73		266.50	266.50	
Weightman, William	48,981.03	49,077.16		2,693.45	2,693.45	
	$176,489.61	$175,559.00	($57.55)	$8,100.03	$8,042.48	
Entertainment Funds						
Harte, Richard H.	$4,690.57	$4,666.01	($1,788.92)	$407.64	$198.31	($1,579.59)
Mitchell, S. Weir	7,381.50	7,364.17	951.86	408.40	527.50	832.76
	$12,072.07	$12,030.18	($837.06)	$816.04	$725.81	($746.83)
Miscellaneous Funds						
Abbe, Robert	$8,860.19	$5,737.09	$2,233.30	$390.50		$2,623.80
Wood, Horatio C.	1,164.80	1,051.19	892.75	52.00		944.75
	$10,024.99	$6,788.28	$3,126.05	$442.50		$3,568.55

JOHN B. FLICK, M.D.
Treasurer

List of the College Lectures, 1940

SCIENTIFIC LECTURES

January 3

ARMSTRONG, CHARLES. Studies in Choriomeningitis and Poliomyelitis. (James M. Anders Lecture XV.) (*Transactions & Studies*, April, 1940.)

February 7

SPIES, TOM DOUGLAS. The Vitamin B Deficiencies. (Mary Scott Newbold Lecture XLVI.) (*Transactions & Studies*, April, 1940.)

March 6

COBURN, ALVIN F. Faulty Disposal of Streptococcus Hemolyticus in Relation to the Development of the Rheumatic Lesion. (Mary Scott Newbold Lecture XLVII.) (*Transactions & Studies*, June, 1940.)

April 3

LUCKÉ, BALDUIN. Tumors in Cold-blooded Animals; their Significance in the Experimental Investigation of Cancer. (*Transactions & Studies*, June, 1940.)

MCFARLAND, JOSEPH. The Diagnosis of Human Cancer. (*Transactions & Studies*, June, 1940.)

May 1

OSGOOD, ROBERT B. The Medical and Social Approaches to the Problem of Chronic Rheumatism. (Nathan Lewis Hatfield Lecture XXIII.)

September 25

CORNER, GEORGE W. The Physiological Basis of Corpus Luteum Therapy. (Nathan Lewis Hatfield Lecture XXIV.)

November 6

FULTON, JOHN F. Neurology and War. (Weir Mitchell Oration VIII. This meeting was not held, but the paper appears in the *Transactions & Studies*, December, 1940.)

*November 8**

ROUGHTON, FRANCIS JOHN W. Flood Storage and Shock. (Mary Scott Newbold Lecture XLVIII.)

HITCHENS, A. PARKER. A Health Program for the Homeside in Wartime. (*Transactions & Studies*, December 1940.)

December 4

WHIPPLE, ALLEN O. Recent Studies in the Circulation of the Portal Bed and of the Spleen in Relation to Splenomegaly. (Thomas Dent Mütter Lecture LIII.) (*Transactions & Studies*, February, 1941.)

LECTURES FOR THE GENERAL PUBLIC

January 19

SCHAEFFER, J. PARSONS. The Human Constitution and Some of Its Problems.

April 12

CHAMBERLAIN, W. EDWARD. The X-ray as an Aid in Diagnosis.

November 15

JACKSON, CHEVALIER. The Bronchoscope.

* Special meeting on medical preparedness, held under the joint auspices of the College and its Section on Public Health, Preventive and Industrial Medicine.

Index to Volume 8

** Communication printed in full.

* Abstract.

The inclusion of the author's name with a subject entry indicates a communication printed in full; subject entries not so accompanied indicate abstracts.

Beginning with this volume, the index will include the names listed in the calendar of officers and committees printed annually in the *Transactions & Studies*. The symbol† indicates that the reference is to the calendar. This should facilitate, in course of time, the gathering of data concerning a Fellow's official connections, if any, with the College.

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